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THE CEREBRAL CORTEX IN MAN

I. THE CEREBRAL CORTEX AND CONSCIOUSNESS *

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A neurosurgeon has a unique opportunity for psychologic study when he exposes the brain of a conscious patient; no doubt it is his duty to give account of such observations on the brain to those more familiar with the mind. He may find it difficult to speak the language of psychology, but it is hoped that material of value to psychologists may be presented, the application being left to them. It seems quite proper that neurologists should push their investigations into the neurologic mechanism associated with consciousness and should inquire closely into the localization of that mechanism without apology and without undertaking responsibility for the theory of consciousness.

To make such an inquiry is to ask a very old question, as is shown by the following quotation from Zophar, the Naamathite, in the "Book of Job":

> Surely there is a vein for the silver
> And a place for gold where they find it.
> .....
> But where shall wisdom be found?
> And where is the place of understanding?

REVIEW OF RELEVANT LITERATURE

The cerebral cortex has apparently acquired increased functional specialization as the mammalian scale is ascended, ending in a remarkable increase in man. Lashley [1] concluded from his work on rats that reduc-

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The words "physiologic," "neurologic," etc., are used in order to conform to the terminology which is compulsory for publication in the ARCHIVES OF NEUROLOGY AND PSYCHIATRY. The author would prefer to use the words "physiological," "neurological," etc.

1. Lashley, K.: Brain Mechanisms and Intelligence, Chicago, University of Chicago Press, 1929.

tion in the capacity of these animals to learn (maze habits) depended on the amount of cerebral tissue which was destroyed. This decrease was not influenced by the nature of the cytoarchitectural fields removed. The function of learning depended therefore, in his opinion, only on the amount of cortical tissue present, not on its anatomic specialization.

Pavlov,[2] working on dogs, concluded that the special function of the cerebral cortex is to establish new nerve connections and so to ensure perfect functional correlation between the organism and its environment. The cortex is, he said, the essential organ for the maintenance and establishment of conditioned reflexes. In contrast to Lashley's findings in the rat, Pavlov admitted that removal of the posterior portions of the cerebral cortex destroyed the activity of the special analyzers for acoustic and visual reflexes, while tactile reflexes were disturbed little. On the other hand, bilateral removal of the anterior half of the cerebral cortex destroyed the analyzer for tactile reflexes and interfered little with the learning and retention of visual and auditory reflexes. He found that removal of both temporal lobes in dogs damaged the auditory analyzer most. Babkin, working in Pavlov's laboratory, showed that after such an operation the dog learned to respond to auditory stimuli consisting of single tones, but that he never reacted to the calling of his name or appreciated successive compound auditory stimuli.

Fulton [3] and his associates, working on monkeys and chimpanzees, have accurately demonstrated a considerable amount of specialization of function in the pyramidal and "extrapyramidal" portions of the cerebral cortex, a specialization which is, to a large extent, exclusive.

In man the increase in specialization of certain areas of the cerebral cortex is as striking as the enormous increase in the total quantity of the cortex. Capacity for replacement, described by Lashley as almost universal in the rat, is still present in man to a considerable extent, especially in infancy. In the adult, however, either occipital lobe is essential to useful vision of any sort in the opposite field; lesions of the motor cortex on one side result in irrecoverable crossed hemiplegia, and the cortical sensory areas on one side are irreplaceable for certain forms of sensation in the opposite limbs. Furthermore, the appearance of speech has resulted in the development of unilateral highly specialized localization within the cortex. The aphasia which becomes permanent after destruction of certain areas of the human brain, still poorly defined, indicates an enormous increase in specialization as compared with the disturbance in the understanding of a dog for compound auditory stimuli after removal of both temporal lobes.

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2. Pavlov, I.: Conditioned Reflexes, translated by G. V. Anrep, London, Oxford University Press, 1927.

3. Fulton, J.: Paralyses of Cortical Origin, Proc. California Acad. Med., 1934, p. 1.

The cerebral cortex of man has been divided into separate cytoarchitectural areas by the histologic studies of Vogt and Vogt,[4] von Economo,[5] Campbell,[6] Brodmann [7] and others, as shown in figure 1. It seems reasonable, a priori, that the differences that exist in the cellular arrangement of these regions should correspond to a difference in function. This is true in the case of the motor and visual areas and must be so to some extent in that of the other regions. That marked substitution is possible in infancy and that some substitution may take place

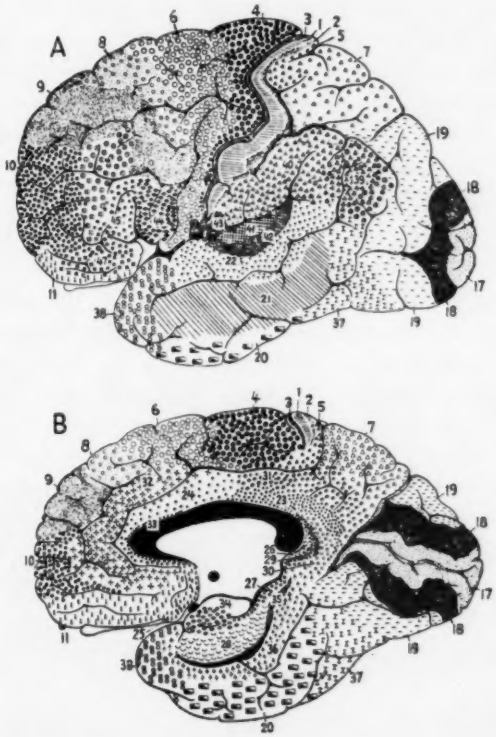

Fig. 1.—Architectural fields of the cerebral cortex (Brodmann).

later do not alter the fact that under normal conditions there is specialization in use of the cortex for special purposes in focal areas.

4. Vogt, C., and Vogt, O.: Die vergleichendarchitektonische und die vergleichendreizphysiologische Felderung der Grosshirnrinde unter besonderer Berücksichtigung der menschlichen, Naturwissenschaften **14**:1190 (Dec. 10) 1926.

5. von Economo, C.: The Cytoarchitectonics of the Human Cerebral Cortex, London, Oxford University Press, 1929.

6. Campbell, A.: Histological Studies on the Localization of Cerebral Function, Cambridge, University Press, 1905.

7. Brodmann, K.: Vergleichende Lokalizationslehre der Grosshirnrinde, Leipzig, Johann Ambrosius Barth, 1925.

Foerster [8] made an effort to delimit function in the human cerebral cortex according to the cytoarchitectural fields of Vogt and Brodmann. This attempt was successful, to some extent at least. In a study [9] of well over 100 cases in which, in collaboration with Dr. Edwin Boldrey, I made electrical exploration of the human cortex, I have been unable as yet to outline functional representation within as sharp limits as those of the cytoarchitectural fields, except for the precentral and postcentral gyri and perhaps the calcarine cortex.

Hughlings Jackson [10] pointed out years ago that recoverability from clinical lesions of the nervous system is chiefly a matter of the quantity of nerve tissue involved, a conclusion startlingly like that reached by Lashley and Pavlov. Jackson, however, described, or rather predicted, three levels of functional differentiation in the central nervous system. The lowest level was to be found in the spinal cord, medulla and pons, where the individual units of the body, such as the muscles, have individual representation. At the middle level, which he suggested would be found in the sensorimotor portion of the cerebral cortex, there was representation not of the individual parts but of peripheral function, such as coordinated movements and elaboration of sensations.

Pavlov, after exhaustive physiologic analysis, arrived at a similar conclusion with regard to the cerebral cortex, which he did not limit to the sensorimotor portion, as Jackson had done. He stated that the entire cortex probably represents a complex system of analyzers of the internal, as well as the external, environment of the organism. He suggested that all tissues of the body will eventually be found to be included in this representation.

Jackson went a step further and inferred that there must be a still higher level of integration, a final sensory and motor arrangement which may form the neural substratum of consciousness; he suggested that this may be found in the frontal and prefrontal regions.

STIMULATION OF THE CEREBRAL CORTEX IN CONSCIOUS PATIENTS

The patients referred to in the following sections were operated on without the administration of a general anesthetic or sedative before operation. Local anesthesia was used to avoid pain, and the brain was exposed widely by means of osteoplastic craniotomy. The operative wound was carefully ringed about and a sheet arranged perpendicularly, so that the patient's face and body were fully exposed below the operative

8. Foerster, O.: The Motor Cortex in Man in the Light of Hughlings Jackson's Doctrines, Brain **59**:135, 1936.

9. Penfield, W., and Boldrey, E.: Somatic Motor and Sensory Representation in the Cerebral Cortex of Man as Studied by Electrical Stimulation, Brain **60**:389 (Dec.) 1937.

10. Taylor, J.; Holmes, G., and Walshe, F. M. R.: Selected Writings of John Hughlings Jackson, London, Hodder & Stoughton, Ltd., 1931.

field. Thus, he could be observed by those who sat beyond the sterile barrier and could converse with them.

Response is obtained from the human cortex most easily from the vicinity of the central fissure of Rolando, that is, from areas 4 and 6 of Brodmann anteriorly and areas 1, 2 and 3 posteriorly (fig. 1). These responses are not obtained from exactly fixed areas, like the keys of a piano, but vary considerably from one patient to another. During a specific operation the sites of elicitation remain constant, but the responses can be influenced by facilitation and inhibition. Outside the motor cortex, the same area in different brains may show marked differences in response, depending apparently on the frequency of some previous experience, such as the aura of an epileptic seizure. These unusual responses may well be explained by the process which Pavlov termed "conditioning."

VOCALIZATION

The discussion may best be opened by a description of vocalization, which I have produced only recently, since I have begun to use a thyratron stimulator. It has not previously been described as an isolated phenomenon in man, and Leyton and Sherrington [11] observed that they could not produce it in anthropoids with faradic stimulation. Friedman [12] produced barking in a dog by stimulation of the motor gyrus. Gibbs and Gibbs [13] produced purring in cats by stimulation in the vicinity of the infundibulum.

CASE 1.—H. M., an intelligent man aged 32, a railroad fireman, had complained of epileptic seizures for three years before admission to the hospital. The cause of these seizures was found to be a small glioma of benign type deep in the frontal lobe near the midline and anterior to the motor gyrus (fig. 2, *T*). In April 1935 the right hemisphere was exposed by osteoplastic craniotomy, and careful experiments with stimulation were carried out. Figure 2 shows a photograph of the cerebral cortex of the patient during operation. He was quiet and cooperative and talked freely with the operator and with the specially trained observer, Miss Mary Roach. The numbers on the small paper squares which may be seen on the surface of the brain indicate the order in which stimulation with positive results was carried out—*1* representing the first stimulation, *2*, the second, and so forth. The rest of the exposed brain was explored completely with the electrode without result.

The positive results of stimulation were as follows: When point *13* was touched with the electrode the patient reported a sensation in the little finger of the left hand. Extension of this finger was observed. This was repeated twice without warning with the same result. At *1*, a feeling of "electricity" was produced

11. Leyton, A., and Sherrington, C.: Observations on the Excitable Cortex of the Chimpanzee, Orangutan and Gorilla, Quart. J. Exper. Physiol. **11**:135, 1917.

12. Friedman, E.: Neurological Aspects of Hoarseness, New York State J. Med. **34**:1, 1934.

13. Gibbs, E., and Gibbs, F.: A Purring Center in the Cat's Brain, J. Comp. Neurol. **64**:209, 1936.

in the left middle finger. No movement was associated with the sensation. At *2*, a feeling of "electricity" was produced in the left index finger; at *11*, there were flexion of the left arm and forearm and extension of the fingers. Stimulation of the last point was repeated, with the same result.

Stimulation at *10*, produced closure of the left hand. The patient reported feeling a strong sensation "like holding on to electricity," meaning that his hand tingled while it closed. At *3*, there was a sensation over the lower lip on the left side. At *4*, a sensation like electricity was produced in the left side of the tongue. Stimulation at *6* produced violent swallowing, and after a short interval of silence the patient stated he had felt "electricity" in the mouth. Stimulation at *7* produced a sensation in the mouth.

These numbers are seen to lie on either side of the central fissure of Rolando. There is no way of determining the central fissure in a living patient except by stimulation because of the great variability in cortical pattern, especially in

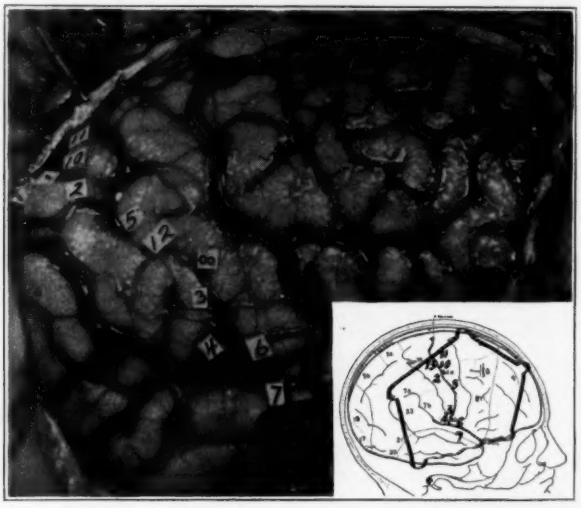

Fig. 2.—Cerebral cortex of H. M., photographed during operation. The numbers placed upon the brain indicate points from which motor or sensory responses were obtained by stimulation. *T* indicates the position of an oligodendroglioma. The inset shows the position of exposure during craniotomy.

pathologic conditions. Point *7* lies just below the fissure of Sylvius; point *6*, just above it. On the precentral gyrus, at point *5*, which lies between two areas from which were produced movements of the upper extremity and of the face, respectively, stimulation resulted in vocalization. Because this was the first example of such vocalization, stimulation of this point was repeated thirty-one times, without causing undue fatigue.

At the first response the patient emitted a somewhat groaning "Oh." After stimulation stopped, he said: "I do not know why I made that noise." This was repeated four times, with the same result. The intensity of thyratron stimulation was 28, the frequency of the stimulus being between 60 and 70 per second. When the patient was asked why he continued to make this noise, he said: "I don't know. Something made me speak, and I felt something touch up there." This

sensation of touch may have been due to pressure on the unanesthetized scalp. The next time stimulation was done he said: "You must have made me do that." The same strength of stimulus produced numerous sensory results in the other areas of the cortex, but no other motor response.

At the seventh stimulation Dr. Colin Russel observed the patient carefully during the vocalization. He remarked that the mouth opened widely, without any expression of fear or emotion during crying. At the eighth stimulation the patient vocalized loudly; when he was asked afterward whether he had felt anything, he said: "Felt anything! Sure, it felt as though you were pulling the voice out of me!" The longer the stimulation was continued the louder the tone and the higher the pitch seemed to become. I prolonged the fourteenth stimulation to study the effect. In this instance, vocalization continued for six seconds and ended in a tremolo (probably when the breath gave out). On one occasion the patient vocalized, then drew a deep breath and continued to cry.

At the eighteenth trial area *12*, about 6 mm. below area *5*, was stimulated, a somewhat stronger stimulus being used. Stimulation of both areas was repeated on the twentieth trial, and it was noted that the tone of the voice was higher at area *5* than at area *12*; the effort, however, seemed greater when *5* was stimulated, which may account for the higher tone.

On the twenty-second stimulation the patient was informed that he was to try not to call out when the stimulus was applied. He said he would try. I warned him when I was going to apply the electrode, but the vocalization began almost immediately after stimulation and continued until the electrode was withdrawn. I then said to the patient, "I win"; he replied, "You did," and laughed. He added: "I guess I would have won if I had been on that side of my head."

In general, the patient was unable to stop the cry or to influence it in any way. He was as surprised at the first sound of his own voice as we were, and he dissociated himself from this artificial employment of his cortex at once. He knew he had not willed it.

With stimulation at a distance of 1 mm. from a circumscribed area, a monopolar electrode being used, no result was obtained, but when the electrode was moved 1 mm. nearer the vocalization occurred regularly in typical fashion. With a stimulus of the same intensity as that used to produce this vocalization no motor movements could be obtained anywhere. Above this point, on the same convolution, stronger stimulation had to be used to produce flexion of the hand, and below the same point stronger stimulation produced violent swallowing. On return to the area of vocalization, even the strong stimulus produced no additional associated motor movements, but only the sound of the patient's voice in the vowel "O" or "A." There was nothing at any time to suggest words.

At ward rounds, nine days later, the following note was made on the patient's record: "When I discussed with the patient his sensation at the time that vocalization was produced on the operating table, he stated that it sounded not as though he was saying anything he wanted to say but as though his voice came with a rush, as something beyond his control. There was no sensation of the mouth, tongue or face at the time of vocalization. He said he felt no sensation anywhere, but 'just as though something drawed it out' of his mouth.

"He dreamed on the day after operation that some one was making him speak but that he did not seem to be on the operating table. There is at present no disturbance in speech, nor has there been since operation."

In 5 subsequent cases vocalization was produced by stimulation of the cortex in an area on the precentral gyrus roughly corresponding to

that in case 1. The locations of the points of vocalization in all 6 cases (in 2 of which they were on the right side) are transposed to the left hemisphere, as shown in figure 3.

CASE 2.—H. Mi. was an intelligent man aged 27. Stimulation of the precentral gyrus produced vocalization (*II*, fig. 3). On the same gyrus above the area stimulation produced symmetric elevation of both brows, and below the area, swallowing.

CASE 3.—F. R. gave vocalization after stimulation of a similar point (*III*, fig. 3), which lay just anterior to points at which sensations in the mouth and tongue could

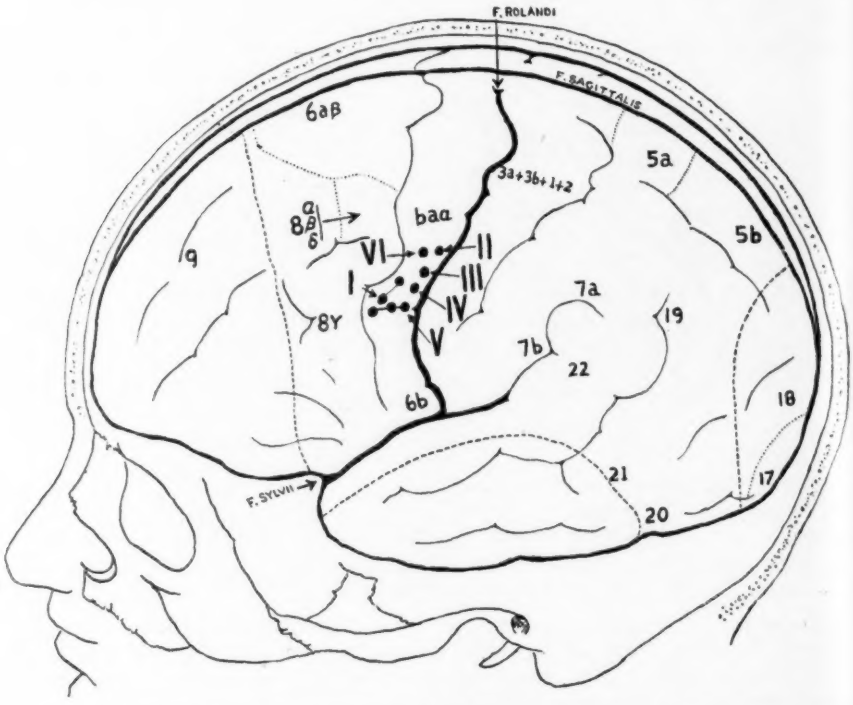

Fig. 3.—Chart showing localization of points from which vocalization was obtained in 6 cases. The roman numerals indicate the numbers of the cases as they appear in the text.

be produced. The area was below the locus for movements of the right eye, but it was not as discrete as that in case 1 and was associated with drawing of the face to the right and a feeling of nausea. This spread was doubtless due to an epileptic habit, as stimulation 2 cm. anterior to and below this point produced an epileptic seizure which resembled those from which the patient habitually suffered and at the beginning of which there was an epileptic cry.

CASE 4.—F. W. was a youth aged 17. Vocalization was produced from the left hemisphere at *IV* in figure 3, just below an area from which closure of both eyes was produced. When the patient had closed both eyes, he remarked that he

could not help closing the right eye. The point of vocalization was just anterior to the source of numbness in the right side of the tongue.

CASE 5.—E. L., a housewife aged 39, had suffered from epileptic seizures for six years after a vascular accident. This vascular lesion had produced the cyst seen in figure 4, situated in the left parietal lobe. There was no aphasia, but the patient was slightly childish.

The central fissure was mapped out by thyratron stimulation, as may be seen in figure 4. The inset indicates the cerebral localization.

Stimulation of *A* produced a pricking sensation in the fingers of the right hand; of *B*, shaking of the entire right hand; of *C*, sensation in the fingers of the right hand; of *D*, sensation in the nose; of *E*, sensation in the right thumb and closure of the jaw; of *F*, sensation in the right side of the chin; of *G*, sensation in the tongue and chin; of *I*, flexion of the elbow; of *H* at the left, flexion of the fingers,

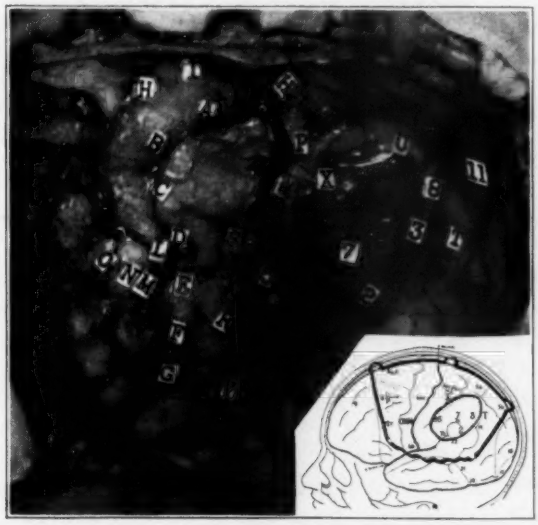

Fig. 4.—Photograph during operation of the brain of E. L., a woman aged 39, who had had occlusion of a cerebral artery six years previously, leaving a deep cyst. The roof of the cyst was a translucent membrane, and the floor, the ependyma of the underlying ventricle. The inset indicates the localization of the cyst.

and of *L*, slight tremor in the right side of the face, with a sensation in the right cheek and the chin.

Stimulation of *M* produced "Umgh." The patient then said: "What is that?" Without replying, I repeated the stimulation. The localization was repeated, and the mouth was pulled to the right. I then asked the patient why she made that noise. She replied that her chin hurt. Stimulation of *N* gave vocalization in the same tone, but in a clonic manner, as though it was regularly interrupted. At *O*, vocalization was in a definite tremolo. The patient was saying: "I can't do . . . ," and carried the "do" over into the sound of vocalization as the area was stimulated. When asked again why she made that noise, she replied: "I don't know."

Stimulation of *O* was repeated for a longer period. Vocalization resulted until the patient's breath seemed to be exhausted, whereon a small epileptiform attack,

consisting of pulling the nose, mouth and face to the right and inward rotation of the right arm, was reported.

The diameter of the area (*M, N* and *O* in figure 4, or *V* in figure 3) from which vocalization was obtained was not greater than 6 or 7 mm. It was observed that stimulation at *O* produced a sound different from that at *M*. It was discontinuous, so that it sounded like speech, but one could not make out words.

When the patient was told to count to 20, stimulation at a little distance did not influence the counting. When the electrode was brought nearer she seemed to continue the "eleven" sound. Stimulation below *M* during the counting caused her to stop on two trials. When asked why she stopped, she replied, "I tremble so."

Electrical exploration was continued; it is interesting that sensation in the chin and right side of the face, which was found to accompany vocalization when *M* and *O* were stimulated, was produced by stimulation at a distance, over the surface of the cyst at *T, 5* and *7*, with no vocalization. Stimulation at *2* and *3* produced sensation in both sides of the face and in the chin and tongue and slight closure of the mouth in a clonic manner. The stimulations just mentioned were made on the translucent covering of a cyst filled with fluid. After removal of the cyst, this translucent material was observed still to contain nerve fibers. This is an example of the spread of excitability that so often is observed in cases of epilepsy. It may perhaps be called epileptic facilitation. In this case it is evident that it was produced by activation of superficial nerve fibers which crossed the surface of the cyst to the postcentral convolution at *F* and *G*, as there was no gray matter and no other fiber layers.

CASE 6.—E. M. was a woman aged 22. Vocalization was produced from the left precentral gyrus (*VI*, fig. 3) in an area no greater than 3 or 4 mm. in diameter. The cry was somewhat quavering and was produced three times. Above it, flexion of the wrist was obtained, and below it, twitching of the lower lip and jaw, more pronounced on the right side.

GENERAL OBSERVATIONS ON CORTICAL STIMULATION

Simple movements, when they are produced, appear to the patient to be quite involuntary. In our whole series of patients, we found none who was under the impression that he was carrying out these movements of his own volition. A public school teacher remarked with regard to the movement that had been produced in her face: "It seems involuntary." Another intelligent young woman observed: "My leg moved itself." Likewise, sensation when produced electrically was referred at once to the periphery as an unexplained sensation.

I have often asked a patient to make an effort not to move the hand, face or foot and have followed this by stimulation of the motor area for this part. The result is usually a movement over which he has no control, and he is not at any time in doubt about this. With or without warning, restimulation of that area will ordinarily reproduce the same movement.

On the other hand, a patient is sometimes able to prevent a movement by an act of will power. In the case of F. W., stimulation of area 6a beta of Brodmann, which Vogt named the frontal adversive

field, produced closure of the right hand and a feeling of heat down the right side of the body. The patient was instructed to make an effort to keep his right hand still if he could. Stimulation was repeated without the patient's knowing when it was to be done. He reported the same feeling of flushing on the right side of the trunk and held his hand still. An example of a somewhat more complicated effort to oppose the effect of cortical stimulation follows.

In the case of an intelligent girl, H. T., the cortex was stimulated anterior to the lower end of the right precentral gyrus while she was counting from 1 to 40. At the time of stimulation the patient hesitated slightly, and the observer reported that there was pulling of the mouth to the left. She continued to count, however. When her task was finished, she said to me: "It was hard to continue." She was able, therefore, to continue to count, although the left side of the mouth had been forced into involuntary movement by stimulation of the right cortex.

Patients sometimes state that they have a strong desire to move which they are able to, or at all events do, control.

F. S., an Italian who found difficulty in expressing himself in English, after subjection to stimulation at nearby points in area 6a beta (fig. 3), made the following observations: 1. "My nerves shook all over; wanted to pull me to the left." (He showed agitation probably because he thought he was about to have a habitual epileptic fit). 2. "Wanted to fall to the left side." 3. "Head feels like it wants to move down to left leg, and left leg up to head."

After R. M. had been subjected to stimulation in the same area, Vogt's frontal adversive field, he said that he had felt as though his "eyes were going to turn to the left." There was, however, no turning of the eyes at that time.

H. T., after stimulation in the same field on the right side, said she wanted to turn her head to the left. She made no obvious movement.

J. H. tried to resist movements produced by stimulation of areas 4 and 6 of Brodmann, without success. However, stimulation at a distance produced downward plantar flexion of the opposite foot, together with the aura of a habitual attack. This stimulation was repeated without warning, and the patient explained that it made him desire to move the foot down. He was asked to resist the desire, and stimulation of the same point was repeated. The patient's foot moved upward, in the opposite direction, and the whole leg was drawn up, in an exaggeration of opposition.

On the other hand, a patient at times may have the feeling of movement without there being any observable change in position of the part.

F. W. stated that at the time of stimulation of the left postcentral lobule he had a sensation of movement in the right thumb. No movement in the thumb could be seen, however. After stimulation was repeated later at this point, without warning to the patient, he reported the same sensation.

Stimulation may sometimes produce a feeling of paralysis in a part without any objective change in the appearance of the part.

H. Mi., after stimulation in the left postcentral lobule, reported that he felt a tremor in the right side of the upper lip and that he lost control of the lip.

There was no obvious movement. When the right precentral lobule was stimulated, H. T. reported that she was unable to speak or to open her eyes. This stimulation was made at a point just below an area where marked closure of both eyes had been produced.

This sort of response may indicate the production of an inhibitory discharge.

When a sensation is produced from stimulation of the cerebral cortex, it is usually described as numbness or electricity. Exceptionally, the patient uses an adjective which suggests a feeling of cold or warmth.

D. R., an intelligent boy, was subjected to stimulation of the left postcentral region of the cortex. He reported that he felt something cold on the right side of the mouth, both inside and out, although stimulations elsewhere produced what he called "electricity," or a sticking sensation in various parts. The feeling of heat down the side has already been reported in the case of F. W.

Pain has been produced by stimulation of the cerebral cortex, particularly in the frontal adversive field, but this has been in relation to the aura of an epileptic seizure, which it may be better not to discuss at this time. Stimulation of the olfactory lobe causes the patient to exclaim with surprise that he smells something.

E. M. said the odor resembled that of oxygen. F. R. said that it smelt like "something burning."

More complicated sensations may also be produced. For example, J. C. said that she felt afraid and had a sensation in the abdomen when the anterior end of the second temporal convolution was stimulated. The next stimulation, at an adjacent point, produced a train of phenomena which must be considered as epileptiform but which illustrate a number of points previously made. The patient had first a sensation in the abdomen, next the feeling of fear and then a desire to move the left hand. There was a plucking movement with the left hand. When she was asked, "Why do you move your left hand and not your right?" she replied, "That one wants to." She added that the movement was "involuntary." This stimulation was repeated several times without warning, with the same result. On one occasion she was warned that the stimulation was coming and was urged to keep the left hand still if she could. On this occasion she reported that she had the same sensation, but kept her hand still. During this stimulation she cried a little; afterward she said she wanted to move her hand, but prevented herself from doing so. It should be added here that the sensation in the abdomen and the feeling of fear were phenomena which sometimes appeared in the epileptic seizures to which this patient was subject.

What do these observations indicate concerning the relation of consciousness to the cortex? Crude motor movements are made by stimulation of the pyramidal and parapyramidal cortical motor areas, but the subject is fully conscious that he has not made them—he has not willed them. He says, rather, that it was involuntary or that the hand moved itself. If a bit of sensory cortex is activated, the patient feels a crude sensation in the hand, but it never occurs to him that he has

imagined it. He hears his own voice crying as the result of stimulation, and when he has finished he exclaims in surprise that his voice was drawn out of him; the next day he may live over the experience in a dream that some one is making him speak.

As far as he is able to go through introspection, the patient concludes that the activity of his own stimulable cerebral cortex is on a plane quite distinct from that of his conscious thinking. The electrode of the surgeon may provide him with a new sensory experience, or it may initiate a motor movement against which he is able to struggle by means of such other cortical mechanisms as are still at his disposal.

Before further generalization, a brief consideration of certain aspects of epilepsy may be interposed.

EPILEPSY

"Epilepsy," Hughlings Jackson said, "is the name for occasional sudden, excessive, rapid and local discharges of grey matter." As this discharge may take place in different areas of the nervous system, so the character of the discharge may vary greatly from movement to sensation and from dream state to mental lapse. In general, however, the movements are violent and purposeless, the sensations crude and the dreams simple.

Jackson conceived that during a seizure there is a discharge in the gray matter of the brain which begins at a local point and spreads from that point, producing a march of outward phenomena. This conception had two results. First, it provided a hypothesis for the understanding of epilepsy. Second, it provided Jackson with a key to the localization of function in the brain. From the study of epileptic patients, he concluded that cerebral convolutions represent the function of certain peripheral parts. He reached this conclusion ten years before Hitzig and Ferrier demonstrated this to be a fact by electrical stimulation of the convolutions of animals.

Consider as an example the jacksonian seizure, which begins by localized movement of the great toe and spreads in succession to the leg, arm, hand and face of the same side. The discharge of the pyramidal cells in the toe area of the precentral gyrus spreads progressively downward through the length of the gyrus. In so doing it maps out the contiguity of cortical representation of these parts. The spread is from one area of gray matter to another, rather than along internal association pathways to more distant centers.

Another example may be cited. An epileptogenic focus in the posterior part of one temporal lobe (Penfield [14]) produced in a patient the following habitual chain of phenomena: (1) hearing of a roaring

14. Penfield, W.: Focal Epileptic Discharge in a Case of Tumour of the Posterior Temporal Region, Canad. M. A. J. **33**:32, 1935.

noise, (2) a sense of dizziness, (3) salivation and (4) micropsia, or the hallucination that everything looks small. Of these phenomena, two were sensory; one was motor, and one, hallucinatory. Discharge of certain areas of the brain produced each phenomenon, but the spread took place in this manner not because special association pathways exist between these areas but because of contiguity of representation.

Epileptogenic discharge of ganglion cells is sudden, overwhelming and undiscriminating, as though they were for the moment affected by a miniature hurricane. The result of this focal hurricane indicates that there exists focal representation in the brain and shows which areas are neighbors. The site of the initial discharge must be sought by the clinician. The cerebral cortex apparently is not the only region where epileptic discharge may take place. It may involve the gray matter at other levels in the central nervous system, including the diencephalon and midbrain, and even on rare occasions the spinal cord.

An epileptic seizure is in some ways the direct opposite of paralysis. A unilateral seizure is on some occasions followed by unilateral paralysis, which usually affects the part that was earliest and most severely involved in the seizure. This postseizure paralysis may consist in monoplegia, hemiplegia, aphasia or mental stupor, or even complete coma and diplegia.

The cause of postseizure paralyses was thought by Jackson to be fatigue of the discharging cells. It was suggested by Kinnier Wilson to be a phenomenon of after-discharge inhibition. The present evidence suggests that these paralyses are due to postconvulsive spasm of the cerebral arteries, or at least to the focal cerebral anemia which frequently follows epileptic seizures of whatever variety (Penfield [15]).

The important point to be borne in mind is that, except during complete coma and diplegia, these paralyses are due to focal or local inactivity of nerve cells, just as the epileptic discharge is due to regional activation of the same cells. Thus, the postepileptic negative state may have for the present purpose a localizing value similar to that of the positive local discharge of a focal epileptic seizure.

It should be remembered, further, that there is paralysis of voluntary function in any part of the brain during epileptic discharge in that part. If it is an area which is too complex to express itself during the discharge there will be no evidence of the fit other than absence of function. A discharge occurring within the speech area signalizes its occurrence only by silence, by the inability to speak. This has the same outward effect as postepileptic paralysis, although the cause is different.

Epileptic disturbances of consciqusness will be considered under the headings of "dream states" and "automatism." Further discussion of

15. Penfield, W.: The Evidence for a Cerebral Vascular Mechanism in Epilepsy, Ann. Int. Med. **7**:303, 1933.

loss of consciousness associated with epilepsy will appear in the final section, entitled "General Considerations."

DREAM STATES

Jackson applied the term "dream states" to alterations of consciousness which appear in epileptic states—alterations without loss of consciousness. In a dream state a patient may have a sudden feeling of strangeness, of unexplained familiarity; some capacity, however, is retained for conscious insight, and he may know that he is having a fit. He may suddenly see a complicated scene, which in fact comes from some past experience, but he can still reason and is aware of the unreality of the condition. Jackson called this double awareness "mental diplopia."

An example of such a dream state may be given in detail.

J. V., a girl aged 14, from the age of 11 had suffered from epileptiform seizures characterized by sudden fright and screaming, when she held on to people for protection. This was followed by falling and occasionally by a major convulsion. In infancy, after an anesthetic, she had had a single convulsion, followed by coma and transient left hemiplegia.

After a typical, but severe, seizure which was induced after admission to hospital, she had transient weakness and a Babinski sign on the left side. On careful questioning, it was learned that during the preliminary period of fright she invariably saw herself in a scene that she remembered to have occurred at the age of 7 years.

The scene was as follows: A little girl was walking through a field where the grass was high. It was a lovely day, and her brothers were walking ahead of her. A man came up behind and said: "How would you like to get into this bag with the snakes?" She was very frightened and screamed to her brothers, and they all ran home, where she told her mother about the event. The mother remembers the fright and the story, and the brothers still recall the occasion and remember seeing the man.

After that, she occasionally had nightmares in which the scene was reenacted. Three or four years later, at the age of 11, it was recognized that she had attacks by day, in which she habitually saw the scene of her fright. She saw a little girl, whom she identified with herself, in the now familiar surroundings. She was conscious of her environment at the time of the attack and called those present by name; yet she saw herself as a little girl with such distinctness that she was filled with terror lest she should be struck or smothered from behind.

At operation, with the use of local anesthesia, adhesions between the dura and the arachnoidea were observed, indicating an old subdural hemorrhage and cortical atrophy, which was most marked in area 19 of the occipital lobe, the region from which the curious complicated aura could be reproduced. This change was probably due to a hemorrhage in infancy, at the time of the anesthesia.

The central fissure was mapped out as seen in figure 5, from *Y* to *M*. Stimulation at points *13* and *17* caused the patient to see stars on the opposite side. At points *16* and *14*, the aura of an attack was produced. After stimulation at *16* she said: "Wait a minute, and I will tell you." A little later she said: "I held on to the bar [as she had been asked to do], and the bar seemed to be

walking away from me. I saw some one coming toward me, as though he were going to hit me." In a moment she called: "Don't leave me." The point *14* was stimulated without the patient's knowledge. She suddenly said: "Say something"; then, a little later: "I had the funny feeling. It was like an attack."

At a point nearby, but from which the mark was accidentally displaced before the photograph was taken, stimulation had previously produced the first aura. She stared suddenly and then cried: "Oh, I can see something coming at me! Don't let them come at me!" She remained staring and fearful for thirty seconds, although the stimulation was of much shorter duration. A little later she said: "It didn't feel like an attack at first, but right after it felt like an attack coming on; it sort of started and then passed off; first time it has felt like an attack since last Wednesday." Wednesday had been the day when several seizures were induced.

Stimulation was carried out at a number of points extending from the first temporal convolution backward through cortical area *22* to the site of the origin

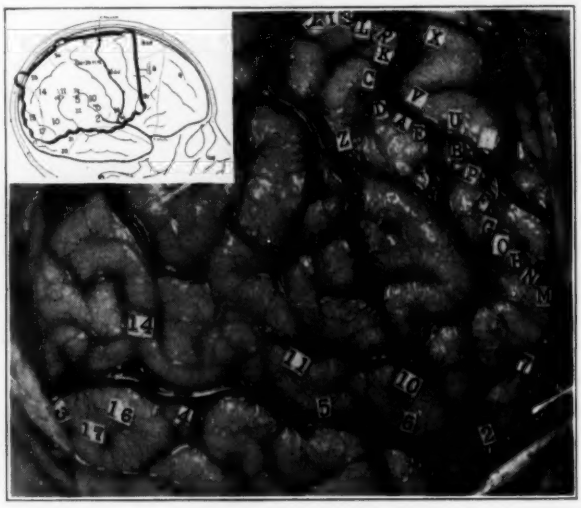

Fig. 5.—Photograph during operation of the brain of J. V., a girl aged 14, who suffered from epileptiform seizures ushered in by a complicated aura, which could be initiated by electrical stimulation at points *14* and *16*.

of the aura in area *19* (fig. 1). These stimulations caused the patient to cry out that she heard a large number of people shouting. Once she said: "They are yelling at me for doing something wrong; everybody is yelling." On inquiry, she said she could hear her mother and brothers. Stimulation at *2* (fig. 5) caused her to say: "I imagine I hear a lot of people shouting at me." The stimulation was repeated twice without warning, for not over two seconds. Each time the voices were heard again, the duration of the voices being eight and seven seconds, respectively. A third time the stimulation was repeated without warning, and she said: "I hear them again." After stimulation at *10*, she cried: "Oh, there it goes; everybody is yelling," and, after an interval, "Something dreadful is going to happen." Stimulation at *11* produced: "There they go, yelling at me; stop them!"

If the epileptogenic discharge began at *16* or *14* and passed forward over points *11, 10* and *2*, she would have had the typical hallucination, felt the dread and eventually heard accusing voices before any convulsive phenomena were observed. As she did not remember the voices in an ordinary seizure, it is likely that she had amnesia for this part of the march, not an infrequent occurrence in this region.

This case is an example of the reproduction of a complicated memory picture of an event which actually occurred between the time of receiving an injury to the brain and the onset of the seizures. This case is not without precedent. I studied a patient whose attacks originated somewhat farther forward in the temporal lobe, as proved by stimulation, and who saw herself giving birth to a child during the aura. The picture she saw reproduced the surroundings of the event as it had actually happened.

A somewhat different type of complicated aura may be mentioned briefly.

M. B., an intelligent woman aged 30, suffered from epileptiform attacks characterized by (1) a hallucination of being far away or of seeing things as small, (2) dizziness or a sensation of turning, (3) tinnitus and (4) numbness in the right hand, all of which were followed at times by loss of consciousness and a generalized convulsive seizure. At operation, in area 5b a somewhat yellowish, soft convolution was observed, and from this convolution and its vicinity the aura could be reproduced. In figure 6 the numbers *3* and *4* are laid on this area.

Stimulation of the postcentral convolution at *1* produced numbness in the thumb, and at *2*, numbness in the right side, from the axilla to the umbilicus; stimulation at *4* produced: "Felt like I was going far away; sometimes like that before an attack. Like when things look far away." After stimulation at *3*, there was dizziness, "like before an attack." With the electrode at *15*, she "felt as though I was falling out of bed." The stimulation was repeated without warning. She said suddenly: "Yes, the same thing; felt as though I was falling."[16]

If the epileptogenic disturbance had begun at *4* and moved to *3*, then to *15* and finally to *2* and *1*, the patient might well have complained first of a hallucination of being far away, then of dizziness, then of falling and, finally, of numbness in the right hand. If the disturbance had spread still farther forward, there would have been convulsive movements.

In such cases it may be said that there is an alteration in consciousness, but actually a new phenomenon is being presented to the conscious person. In the case of J. V., this phenomenon arose from a discharge which occurred within the cortex of cytoarchitectural area 19. At the same time, the patient, because she retained consciousness, differentiated between the spurious phenomenon, which might be called synthetic, and

16. Foerster described the similar case of a woman who had an epileptogenic scar in the left parietal lobe near the midline. Stimulation here caused the patient to feel as though she were rolling off the table to the right.

the actual existence of the outside world as presented to her by the unoccupied regions of the cerebral cortex. In the case of M. B., a disturbance originating in area 5b gave her the hallucination of being far away; yet she retained an understanding of her surroundings.

AUTOMATISM

Quite different from the dream state is the postepileptic automatic state. The subject is in full control of his body but does not know what he is doing. He may respond if spoken to. He may obey a command or may resent violently and dangerously any interference.

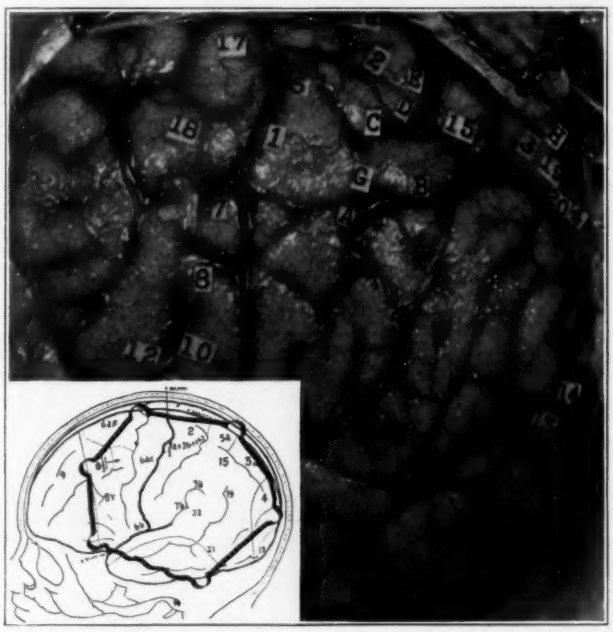

Fig. 6.—Photograph during operation of the brain of M. B., a woman aged 30. Complicated habitual aura could be initiated by stimulation at point *4*.

One may prefer to call this an alteration in consciousness, but it seems to me a loss of consciousness on an exceedingly high level, if the expression is permissible. The patient has no present responsibility, nor will he have future memory of what he does. A brief example may be cited.

An intelligent, sensitive young man gave a history of major seizures, sometimes followed by violent behavior which distressed him as well as his parents. While in bed in the public ward of the Royal Victoria Hospital, he had a seizure during sleep, characterized by convulsive movements on both sides and frothing at the mouth. He then got out of bed and, without putting on slippers

or bathrobe, began to look for something under the bed—possibly his slippers. He walked about and then got into bed with another patient. When the nurse, doctor and prospective bedfellow opposed him, he fought them violently. On coming to himself, he had no recollection of the incident and was chagrined to learn of it.

Jackson expressed the belief that such a state is invariably due to postepileptic paralysis—paralysis of the highest level of neural activity, the substratum of consciousness. He therefore concluded that the state is a phenomenon of release from higher control. If it is in truth postconvulsive paralysis, I suggest, on the basis of what is now known, that effective anemia remains in the region in which consciousness is represented. Sometimes the preceding seizure is slight indeed. At other times there is no evidence of any such seizure. The same is true in other spheres. A hand may become suddenly paralyzed without sign of convulsion, doubtless owing to spontaneous anemia without a preceding epileptogenic reflex.

It is possible, however, that the paralysis is not always postepileptic. If an epileptic fit takes place in the same level or area of the brain as the postepileptic paralysis, automatism must be possible during a fit caused by discharge in this highest level, as well as in the period after discharge. Some petit mal seizures must be of this nature.

GENERAL CONSIDERATIONS

For the purposes of this discussion, it seems unnecessary to inquire into the mechanism by which a conscious decision receives its initial activation in neuronal conduction, or even to inquire whether such decisions are reflex. It is enough to be able to recognize when a person is conscious and when he loses consciousness, to describe what portions of the central nervous system may be paralyzed without abolishing consciousness and what portions may be still active when consciousness is gone. Finally, one may hope to indicate the areas which are necessarily inactive when consciousness is abolished by a paralyzing lesion.

In the dream state of an epileptic patient, as already described, a hallucination is presented to him by discharge within one portion of the cerberal cortex, but the patient retains insight into his real environment, owing no doubt to normal function in other parts of the cerebral cortex. He may even be able to say to an observer (as J. V. did): "Wait a minute," and after the dream is over to recount it in detail. This may, in a sense, be doubling of consciousness, but it is not loss. In the postepileptic automatic state the patient still has cortical mechanisms intact, and, furthermore, he still has coordinating control of these mechanisms. He is a perfect machine, but either he has lost consciousness exclusively or there has been temporary removal of one element of consciousness.

By analogy, this must be produced by paralysis either of a small area of the brain or of scattered mechanisms with a unit blood supply.

Most often, consciousness is lost by these patients in association with certain epileptic phenomena and as a part of the habitual pattern. In general, an epileptic disturbance may spread a considerable distance over the cortex, especially the postcentral portion, before consciousness is lost. On the other hand, loss of consciousness during a true seizure may be primary, without any manifestation other than a blank expression and arrest of speech (petit mal). The return of consciousness in such a patient may be without sign, and he may continue his train of thought without knowledge of the gap. The neurologic mechanism, temporarily inactive, must be the same as, or similar to, that which is paralyzed in automatism.

In a more severe petit mal seizure there are usually, as pointed out by Jackson, certain associated phenomena, such as "deep pallor and a slight wave of universal movement." Such a lapse is sometimes regularly associated with loss of the mechanism for maintaining erect posture, and the patient suddenly falls to the ground. If there is an aura preceding simple loss of consciousness, it is most often epigastric or visceral.

Consider for the moment that consciousness, like movement, vision, hearing and speech, has a localizable representation in the brain. From the nature of the associated phenomena just described, one might suggest that this representation finds its topographic localization near the representation of autonomic function in the hypothalamus, close to the third ventricle, in the region in which blanching of the face may be produced and visceral sense may be represented, and adjacent to the upper end of the nerve circuits in the midbrain which maintain standing. This topographic localization signifies a belief not in a punctate center but in a general region. The exact position may be wrong, but the reasons for searching for such a localization are valid.

I may make another observation on the relation of consciousness and epilepsy. Consciousness is invariably lost at the beginning of the attacks in which the convulsion is generalized from the start. If there is an as yet uncharted area of the brain where all sensory and motor processes are rerepresented, epileptogenic discharge there would result in involvement of all somatic and visceral functions simultaneously and would obliterate consciousness from the beginning.

Hughlings Jackson found this problem a favorite one. He often quoted these words of Herbert Spencer: "The seat of consciousness is that nervous centre to which mediately or immediately the most heterogeneous impressions are brought."

On a lower functional level, vision has its neural mechanism in the occipital lobes, and hearing, in the temporal lobes; that is, a sound produces the neural activity in the temporal lobes which forms the basis of hearing. In the motor region the neural activity forms the basis for voluntary movement. If there were available no other evidence, no knowledge of the anatomic relation of tracts, and an experimental animal had never been used, the study of human epilepsy would have shown these facts concerning voluntary movement, hearing and seeing.

In an analogous manner, the evidence from the study of epilepsy suggests that there is a region where the neural activities converge which are the indispensable substratum of consciousness. The elements are there both for sensation and for the initiation of movement.

However, perhaps it would be well, before one yields to the temptation of anatomic localization, to reconsider the physiologic and psychologic results of cortical stimulation independent of the evidence obtained from the study of epilepsy.

The phenomena produced by cortical stimulation are crude. The movements involve many different muscles, which depend on wide innervation in the brain stem and spinal cord; yet the result is simple flexion or extension of a part or a turning movement which accomplishes nothing purposive. If stimulation of a cortical motor area is carried out during the execution of some voluntary act by the subject, the motor mechanism in question is snatched away from his control, but he may continue to carry out the act if there are other mechanisms available not so stimulated. Thus, H. T. continued to count aloud, even though one side of her mouth was caused to contract in the useless manner of a motor discharge. She said she found the counting hard work, but she succeeded, no doubt owing to the fact that she was using the other side of the mouth appropriately by means of the motor mechanism from the opposite hemisphere.

If, however, vocalization is being produced by stimulation of one hemisphere, the larynx, diaphragm and all the accessory muscles of phonation are preempted by this discharge. The subject cannot speak or alter the vocalization, however hard he may try. A homologous mechanism for vocalization exists in the opposite hemisphere, but the final common path of this discharge has already been preempted by stimulation with an electrode.

The demand of an electrode is not always irresistible. Although stimulation of Brodmann's area 4 or 6 produces a movement which the patient cannot inhibit, stimulation of the brain of an epileptic patient at a distance from the motor cortex sometimes produces what he describes as a desire to move a certain part. By making a conscious effort he can prevent such movement, and in his effort to do so he may, at the time of stimulation, make the opposite movement (J. H.). On the

other hand, if the fingers of one hand are caused to close by an irresistible electrical stimulus, the patient can easily use the other hand in an efficient manner to try to force the fingers open.

An electrode can produce no more evidence of a directed, purposeful, skilful movement than is to be found in the mockery of action produced by an epileptic cortical discharge.

Sensory and hallucinatory phenomena of a more complicated nature may be produced in the posterior two thirds of the hemispheres, but only when these phenomena have previously formed part of a recurring epileptic fit, which seems to prepare that portion of the cortex for local conditioned reflexes. The stimulation seems to reproduce a familiar chord, the harmony of which has become the characteristic expression of that area of cortex when stimulated.

The preceding discussion applies to the sensorimotor cortex. No mention has yet been made of the frontal lobes anterior to areas 4, 6a alpha and 6a beta of Brodmann. This is what Campbell [6] called the frontal and prefrontal cortex (fig. 7). It is dangerous to give this area a name, because of the confusion of terminology that already exists, as pointed out by Walshe,[17] but for convenience of discussion it may be called the extramotor frontal cortex.

In regard to this portion of the frontal lobe, Pavlov wrote that it should (probably) be included with the rest of the cerebral cortex. A clearer impression of his eventual opinion, however, may be gathered from the letter of his pupil, Prof. Boris P. Babkin, who wrote me as follows:

> Many of the experimental data obtained by you in man point in the same direction as the facts obtained by us in Pavlov's laboratory, namely, that the cortex is primarily a representation of the receptors scattered over the external and internal surfaces of the body. However, in the last years of his life, Pavlov came to the conclusion that the frontal region of man serves for higher neural activities than the formation of conditioned reflexes. Thus, if a conditioned stimulus is regarded as a signal, there also may be formed "signals of signals," e. g., words. The "centre" for the formation of these signals of signals would be the frontal region. Pavlov never touched the problem of consciousness. At any rate, in the dog it is not located in the frontal lobes, as I know from my own experiments involving extirpation of this part of the hemispheres.

Hughlings Jackson suggested that in the "prefrontal" area was to be found the highest level of rerepresentation. He suggested this, however, in the same tentative manner that he once suggested, in the days before Hitzig, that motor and sensory representation would be found in the corpus striatum.

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17. Walshe, F.: On the "Syndrome of the Premotor Cortex" (Fulton) and the Definition of the Terms "Premotor" and "Motor," Brain **58**:49, 1935.

In my own experience no convulsive phenomena have been produced by electrical stimulation of the extramotor frontal cortex, and no responses of any sort have been elicited other than what may be called autonomic alterations—and these so rarely as to make conclusion prema-

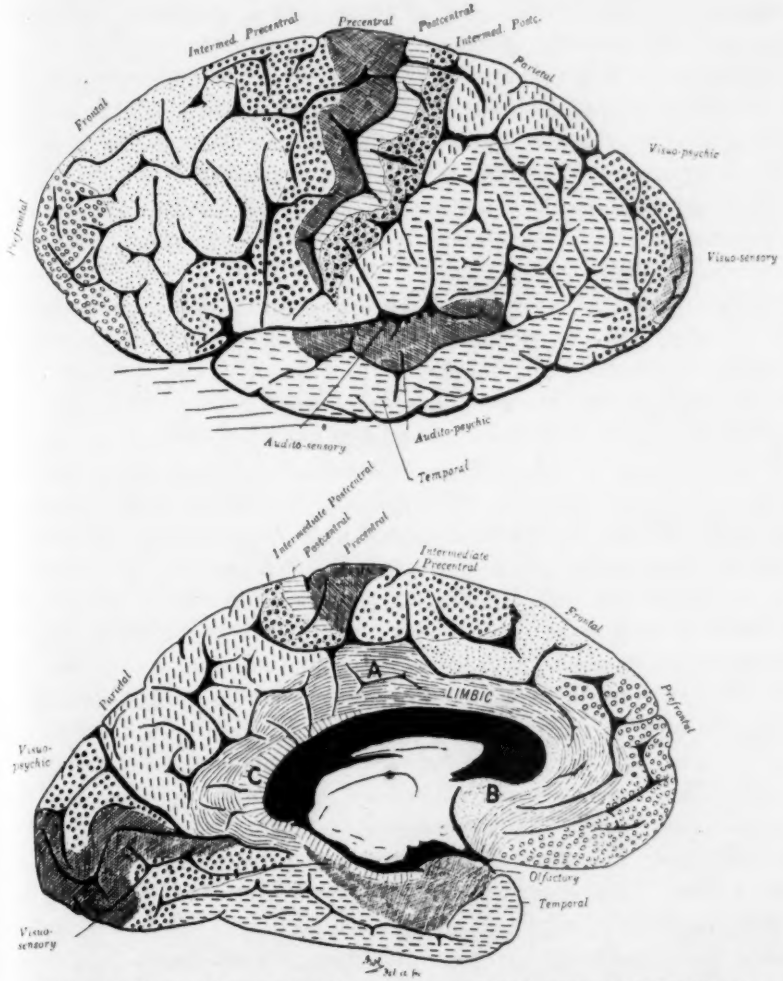

Fig. 7.—Cytoarchitectural fields of the cerebral cortex (Campbell [6]).

ture. Possibly other forms of electrical current may give a different result. So far, here, no alteration and no arrest of consciousness has been produced, even by strong stimulation, and neither effect has been reported by other investigators.

Fits which originate from focal lesions in the frontal pole are characterized, it is true, by initial loss of consciousness, followed by adversive movements before the appearance of generalized convulsions.

Radical extirpation of the whole of one frontal lobe, including all the extramotor cortex and even extending back into area 6a beta, may be carried out in a conscious patient without loss of conscious insight during the procedure or of memory of the details of the event afterward. After immediate recovery, the most important detectable sequel, in my opinion, is "impairment of those mental processes which are prerequisite to planned initiative" (Penfield and Evans [18]).

If this large area of cortex in both frontal lobes were necessary for the existence of consciousness, it is likely that there would be at least temporary loss of consciousness during the removal of one lobe and until the remaining lobe could take over the function of the two. Yet one occipital lobe may be removed without the patient's being aware of any interference with vision or of reduction in the visual field. Furthermore, that epileptiform discharge in the extramotor frontal cortex obliterates consciousness may be likened to the fact that such discharge, if it is strong, in one occipital lobe may produce complete temporary blindness, a blindness that applies to the whole visual field, and the patient says that everything is dark.

All this suggests that the frontal lobes anterior to recognized motor areas are utilized in conscious processes, but that they are not indispensable to the existence of consciousness. It is conceivable that these lobes represent an elaborative field for a more essential concentration of nerve tracts which lies posteriorly and more centrally in the brain. It should be pointed out, however, that stimulation of this area of the brain in man has as yet cast no light on its function; I should like to exclude the extramotor frontal cortex from any conclusions reached here in regard to the rest of the cerebral cortex. Long-continued unconsciousness appears clinically in patients who have a lesion in an area somewhere above, but not far removed from, the midbrain and its vicinity. Details will be omitted here, but twice, after operations on the posterior fossa, patients of mine have passed into a condition eventually resembling sleep, in which they lived several months, with feedings by stomach tube. In another case a similar state, from which the patient began to rouse after six weeks of artificial feedings, followed operative removal of a tumor that extended into the pulvinar. Such localization as has been achieved for sleep, normal and pathologic, also implicates this general region (Hess [19]).

It is of course impossible to state that in such unconscious states as those just described all sense perception is gone. One may conclude no more than that volitional aspects of consciousness are nonexistent

18. Penfield, W., and Evans, J.: The Frontal Lobe in Man: A Clinical Study of Maximum Removals, Brain **58**:115, 1935.

19. Hess, W.: The Autonomic Nervous System, Lancet **2**:1199 (Dec. 3) 1932.

and that no later memory of the state persists. In a discussion of this general field, Prof. Charles Hendel pointed out to me that in one sense I cannot escape the formulation of some definition of consciousness, at least by implication, and that my argument applies particularly to volitional consciousness or the motor element of consciousness. It is true that if there is such a thing as sense perception or pure sensory consciousness in the absence of all volitional capacity, the evidence produced in this study seldom applies to it, and patients have no memory of such a state. Nevertheless, after an epileptic seizure a patient may say he heard and saw what was happening during the seizure but could give no outward sign. The physiologic explanation for this state, it is evident, is that the necessary cortical motor mechanisms were taken away by the epileptic disturbance, while certain sensory cortical mechanisms were not so preempted. At such a time the patient could hardly be called unconscious.

The commonly published conception of the cerebral cortex is that it represents the highest level in the scale of nerve activity. The objective evidence derived from a study of epilepsy and from the observation of conscious patients during operations on the brain supports the view of Hughlings Jackson that the sensorimotor cerebral cortex represents only a middle level of integration.

Man is one of a million species of animals, some of which at least seem to be conscious. Parker [20] pointed out the conservatism of nature with regard to changes in the central nervous system as compared with the radical variety of outward forms. The human cerebral cortex has developed coincidentally with man's acquisition of new skills and new adjustments to his environment. A priori, there seems to be no reason that the neural mechanism essential to consciousness should migrate outward into the newly exfoliated hemisphere.

In a conscious person it must be from somewhere that neuronal impulses pass to the motor areas of the hemispheres, producing complicated behavior which cannot be simulated by electrical stimulation anywhere over the cortex. Hallucinations involving elaborate memory of visual and auditory pictures can be produced by such stimulation, but the patient retains conscious insight into the unreality of the experience. The same epileptic and postepileptic processes which paralyze discrete areas of the cerebral cortex may also abolish consciousness. Therefore, it seems reasonable to assume that there is a discrete area of the brain the integrity of which is essential to the existence of conscious activity.

Finally, there is much evidence of a level of integration within the central nervous system that is higher than that to be found in the cerebral

20. Parker, G.: The Origin, Plan and Operational Modes of the Nervous System, New York, 1934.

cortex, evidence of a regional localization of the neuronal mechanism involved in this integration. I suggest that this region lies not in the new brain but in the old—that it lies below the cerebral cortex and above the midbrain.

Such localization does not signify that other parts of the brain play no role in this mechanism. All regions of the brain may well be involved in normal conscious processes, but the indispensable substratum of consciousness lies outside the cerebral cortex, probably in the diencephalon.

This discussion has avoided the subject of the nature of consciousness. That is a psychologic problem. It has been concerned with the localization of the "place of understanding," and by "place" is meant the location of those neuronal circuits which are most intimately associated with the initiation of voluntary activity and with the sensory summation prerequisite to it.

SWEAT SECRETION IN MAN

IV. SWEAT SECRETION OF THE FACE AND ITS DISTURBANCES

CARL FELIX LIST, M.D.
AND
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The observation of sweating responses affords an excellent opportunity to study the vegetative cutaneous innervation. This is of particular physiologic and diagnostic interest in the region of the face, since other methods, such as observation of the pilomotor and vasomotor reactions, fail to give adequate information.

It has been established that the sweat glands of the face, similar to those of the rest of the body, are innervated by sympathetic fibers, but there is also evidence that a parasympathetic nerve supply exists. A review of the literature reveals considerable disagreement as to the course of the sweat fibers of the face. It is therefore our endeavor in this investigation (1) to trace the course and distribution of the sympathetic sweat fibers from the superior cervical ganglion to the skin of the face, and (2) to analyze sweating responses of the face which are apparently not transmitted by sympathetic fibers. Particular attention will be given to the phenomenon of "gustatory perspiration."

MATERIAL AND TECHNIC OF INVESTIGATION

Material.—This paper is based on 41 clinical observations on selected patients presenting various circumscribed lesions of the nervous system. Since the lesions in a large number of cases were produced surgically (section of nerves or injection of procaine hydrochloride or alcohol), their site and extent were accurately ascertained. In the remaining observations no verification was forthcoming, but the neurologic signs allowed definite localization.

Technic (List and Peet[1]).—All sweating tests were performed by Minor's iodine and starch method. They were of three types: 1. Thermoregulatory

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From the Department of Surgery, the University of Michigan Medical School.

Read at the Sixty-Third Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 3, 1937.

1. List, C. F., and Peet, M. M.: Sweat Secretion in Man: I. Sweating Responses in Normal Persons, Arch. Neurol. & Psychiat. **39**:1228 (June) 1938; II. Anatomic Distribution of Sweating Disturbances Associated with Lesions of the Sympathetic Nervous System, ibid. **40**:27 (July) 1938; III. Clinical Observations on Sweating Produced by Pilocarpine and Mecholyl, ibid. **40**:269 (Aug.) 1938.

sweating. This was the standard procedure used. By this method, sweating is elicited by ingestion of hot fluids and acetylsalicylic acid in conjunction with the application of external heat. The method is particularly suited to study of the function and distribution of sympathetic sweat fibers. Abolition of sweating by this method indicates a lesion of the sympathetic sweat fibers, while increase in sweating may have causes other than sympathetic irritation. For this reason, only cases in which there were destructive nerve lesions have been used for study of the course and topographic distribution of sympathetic sweat fibers. For the analysis of perspiration of nonsympathetic origin the following diaphoretic methods were employed.

2. Sweating produced by subcutaneous injection of parasympathomimetic drugs (pilocarpine; mecholyl [acetylbetamethylcholine hydrochloride]).

3. Sweating produced by gustatory stimulation.

COURSE AND DISTRIBUTION OF SYMPATHETIC SWEAT FIBERS

LESION OF THE CERVICAL PORTION OF THE SYMPATHETIC CHAIN (LIST AND PEET[1])

OBSERVATION 1 (R. J.).—The right superior cervical ganglion was resected for relief from migraine. The heat sweating test showed complete anhidrosis over the right side of the face (fig. 1 *A*).

The complete anhidrosis observed in this instance proves that all sweat fibers for the head pass exclusively through the homolateral cervical portion of the sympathetic chain. The terminal sympathetic neuron for the face begins in the cells of the superior cervical ganglion. Although the postganglionic fibers arising in this ganglion also supply the first three cervical dermatomes, superior cervical ganglionectomy usually produces anhidrosis of the face only because of the supplementary innervation from the middle cervical ganglion.

The postganglionic sympathetic fibers emerging from the superior cervical ganglion reach the face via (1) the periarterial plexus of the external carotid artery and its branches and (2) the internal carotid nerve, which is the principal cranial extension of the superior cervical ganglion. The medial and lateral portions of the internal carotid nerve form the periarterial plexus of the internal carotid artery. The following sympathetic fibers arise from the lateral part of this plexus: (1) the caroticotympanic nerves for the tympanic plexus; (2) the deep petrosal nerve for the sphenopalatine ganglion; (3) fibers for the major superficial petrosal nerve to the geniculate ganglion; (4) fibers for the sixth nerve, and (5) fibers for the gasserian ganglion. The medial part of the carotid plexus continues into the cavernous plexus and sends terminal branches to: (1) the third, fourth and sixth nerves; (2) the first branch of the trigeminus nerve, and (3) the periarterial plexus for the end branches of the internal carotid artery. Thus, the post-

ganglionic sympathetic supply for the head spreads out in a vast network. Of course, not all these anatomically known sympathetic fibers innervate sweat glands. The connections with the third, fourth and sixth cranial nerves, for example, have nothing to do with sweat secretion. Lesions of the cranial sympathetic plexus must be extensive in order to produce definite and localized loss of sympathetic function.

In 1 instance a syndrome was observed which suggested involvement of the internal carotid or the cavernous plexus.

OBSERVATION 2 (C. I.).—For thirty years the patient suffered from attacks of severe unilateral occipitofrontal headache, usually on the right. A definite Horner syndrome was present on the right side. The function of the right fifth nerve was normal. Marked hypohidrosis over the right side of the fore-

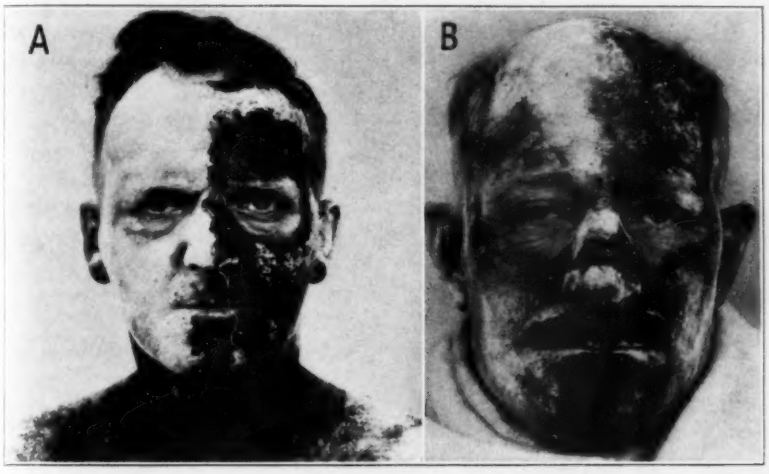

Fig. 1.—Heat Sweating. *A* (observation 1), resection of the right superior cervical ganglion, and *B* (observation 2), syndrome of the right internal carotid plexus.

head (distribution of the ophthalmic branch of the fifth nerve) could be demonstrated by the sweating test (fig. 1 *B*). The diagnosis of a syndrome referable to the internal carotid artery or the cavernous plexus seemed justified in this case, since the regional sympathetic paresis (involving oculopupillary and sweat fibers for the first division of the trigeminal nerve) was not associated with a lesion of the fifth nerve. This observation suggests that the sympathetic fibers for the sweat glands of the forehead and anteroparietal region arise from intracranial end branches of the cervical portion of the sympathetic chain.

LESIONS OF CRANIAL NERVES

In the extremities, the postganglionic sweat fibers are carried by mixed nerves and finally reach the skin via the sensory cutaneous nerves.

A similar arrangement may be anticipated for the sweat fibers of the head. In this section, various lesions of the cranial nerves will be studied with regard to disturbances in sweating.

(*a*) *Lesions of the Fifth Nerve.*—Section of the Sensory Root.

OBSERVATION 3 (M. G.).—Complete section of the sensory root of the left fifth nerve was performed for relief from trigeminal neuralgia. No modification of sweating (normal reaction) was observed after the operation.

OBSERVATION 4 (J. N.).—The patient suffered from trigeminal neuralgia involving the first and second divisions of the nerve on the left. Previously, in another clinic, alcohol had been injected into the second branch. The sweating test before operation showed slight hypohidrosis of the left side of the forehead and left temple; a test after operation yielded the same result.

OBSERVATION 5 (L. S.).—Trigeminal neuralgia involved all three branches of the left nerve. The sweating test revealed minimal hypohidrosis of the left side of the forehead and left temple before operation. On the tenth day after total section of the sensory root more pronounced hypohidrosis was found over the left side of the face, which was most marked over the left side of the forehead and left temple (fig. 2 *A*).

OBSERVATION 6 (E. C.).—Trigeminal neuralgia involved the second and third divisions of the right nerve. The patient had had two injections of alcohol into the third division, without relief. No sweating test was done before operation. Six days following partial section of the sensory root of the right fifth nerve (the ophthalmic division was spared) a sweating test showed definite diminution of perspiration over the entire right side of the face. The hypohidrosis was most pronounced over the forehead and temple and least marked over the chin. The patient was examined a year after the operation. It was then found that sweating was normal and equal on the two sides of the face.

Lesion or Resection of the Gasserian Ganglion.

OBSERVATION 7.[2]—The patient was suffering from a carcinoma of the breast. Complete motor and sensory paralysis of the left trigeminal nerve was present, presumably due to metastasis in the gasserian ganglion. Sweating was normal and equal on the two sides of the face.

OBSERVATION 8 (B.).—A year previous to admission the right gasserian ganglion had been resected for relief from trigeminal neuralgia. The sweating test revealed early minimal diminution of sweating over the right side of the forehead; later it became equal on the two sides (fig. 2 *B*).

OBSERVATION 9 (E. K.).—The patient complained of pain in the second and third branches of the left fifth nerve. Hypesthesia was found in the area supplied by the third division. Several weeks prior to admission the patient had received an injection of alcohol into the left infraorbital nerve, without relief. At operation a neurinoma of the gasserian ganglion was discovered. The entire ganglion with its sensory root was resected, together with the intracranial portion of the third branch. The sweating test after this operation showed normal and equal

2. This patient was previously reported on by Guttmann and List.[5]

3. Footnote deleted on the proof.

sweating on the two sides of the face except for hypohidrosis over the left side of the upper lip caused by the previous injection of alcohol (see observation 15; fig. 2 *C*).

Total section of the sensory root of the fifth nerve, as well as removal of the gasserian ganglion, produces no permanent change in

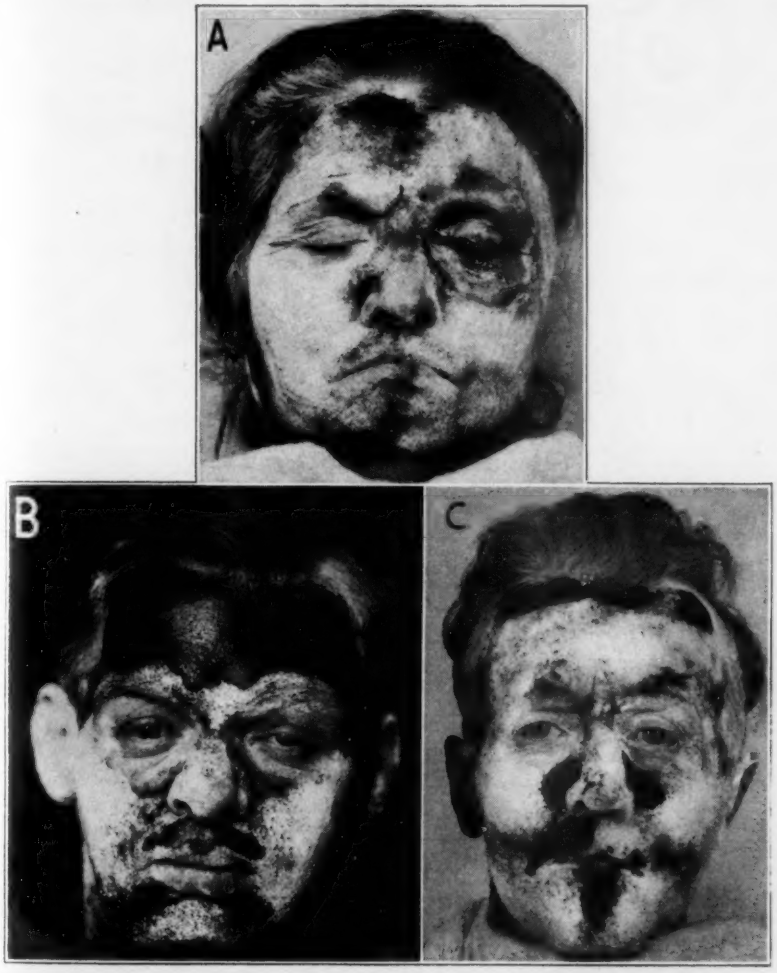

Fig. 2.—Heat sweating. *A* (observation 5), ten days after section of the sensory root of the left fifth nerve; *B* (observation 8), one year after resection of the right gasserian ganglion, and *C* (observation 9), after removal of the left gasserian ganglion for tumor. Note hypohidrosis of the left side of the upper lip following a previous injection of alcohol into the left infraorbital nerve.

thermoregulatory sweating. There may be moderate, poorly demarcated hypohidrosis of the temporal and frontal regions, which is most pronounced shortly after the operation but disappears with time. The

sensory root of the fifth nerve and the gasserian ganglion, therefore, apparently contain few or no sympathetic sweat fibers. The temporary slight hypohidrosis found in the early period after operation may be due to operative injury of the neighboring carotid plexus; if a few

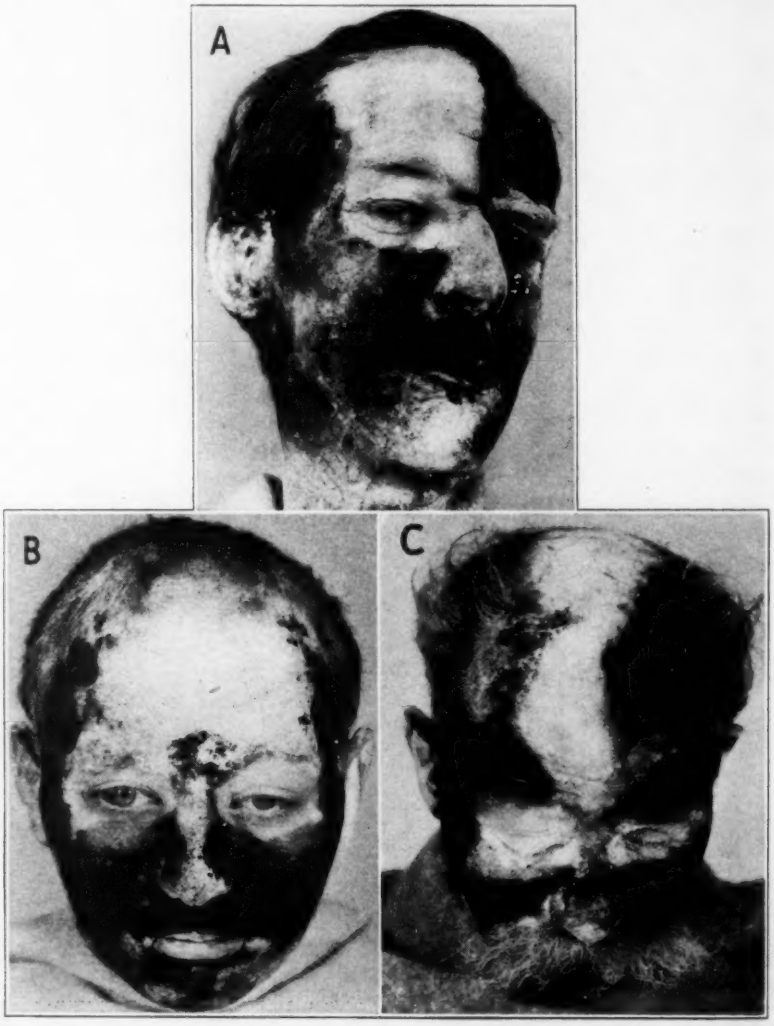

Fig. 3.—Heat sweating. *A* (observation 10), procaine block of the right supraorbital nerve; *B* (observation 11), section of both supraorbital nerves, and *C* (observation 12), injection of alcohol into the right supraorbital nerve.

sympathetic sweat fibers are divided with section of the sensory root or removal of the gasserian ganglion, loss of their function is soon compensated.

Lesions of Extracranial Branches of the Fifth Nerve: First branch.

OBSERVATION 10 (F. F.).—Procaine block of the right supraorbital nerve produced complete anesthesia in the distribution of the nerve. The sweating test showed that complete anhidrosis was confined strictly to the anesthetic area (fig. 3 *A*).

OBSERVATION 11 (P. L.).—Both supraorbital nerves and arteries were completely divided after a compound fracture of the skull at the orbital rim. The sweating test revealed complete anhidrosis in the anesthetic supraorbital area (fig. 3 *B*).

OBSERVATION 12 (C. M.).—An injection of alcohol into the right supraorbital nerve was given for relief from trigeminal neuralgia involving the first division of the nerve. The sweating test showed marked hypohidrosis in the area of anesthesia (fig. 3 *C*).

Second branch.

OBSERVATION 13 (F. F.).—Procaine block of the second branch of the left trigeminal nerve in the sphenopalatine fossa (injection through the palatine canal) was performed. Complete anesthesia of the entire second branch was obtained. The sweating test revealed hypohidrosis over the left side of the upper lip and nose (fig. 4 *A*).

OBSERVATION 14 (D. K.).—An injection of alcohol into the second branch of the fifth nerve at the foramen rotundum was given for relief from trigeminal neuralgia, with resultant complete anesthesia and almost complete anhidrosis of the skin supplied by this branch (fig. 4 *B*).

OBSERVATION 15 (F. F.).—Procaine block of the left infraorbital nerve was effected, with complete anesthesia and anhidrosis in the area of its cutaneous distribution (fig. 4 *C*). Observation 9 may be compared.

Third branch.

OBSERVATION 16 (F. F.).—Injection of procaine hydrochloride into the third branch of the fifth nerve below the foramen ovale was performed. Anesthesia of the entire third branch was produced. Sweating was diminished over the left side of the chin and lower jaw.

OBSERVATION 17 (F. F.).—A submucosal injection of procaine into the third branch of the left fifth nerve near the lingula of the mandible was given. Complete anesthesia in the area of the inferior alveolar and lingual nerves was produced. The sweating test showed complete anhidrosis of the left cheek and the left side of the lower jaw and lower lip; mild general hypohidrosis was present over the remainder of the left side of the face (fig. 5 *A* and *B*).

OBSERVATION 18 (F. F.).—Procaine block of the right auriculotemporal nerve was performed. Complete anesthesia and anhidrosis resulted (fig. 5 C).

The peripheral end branches of the trigeminal nerve contain postganglionic sympathetic sweat fibers. In these nerves the sweat fibers have the same cutaneous distribution as the sensory fibers, the areas of anesthesia and those of anhidrosis being practically identical. The complete anhidrosis which is associated with total lesions of the extracranial branches proves that in the periphery only the trigeminus nerve carries the sympathetic sweat fibers. Thus, the general rule is confirmed that

the sensory cutaneous nerves represent the terminal pathway for the postganglionic sympathetic sweat fibers. The question remains as to where these sweat fibers leave the cranial sympathetic plexus to join the trigeminal branches. It is probable that most of the sweat fibers

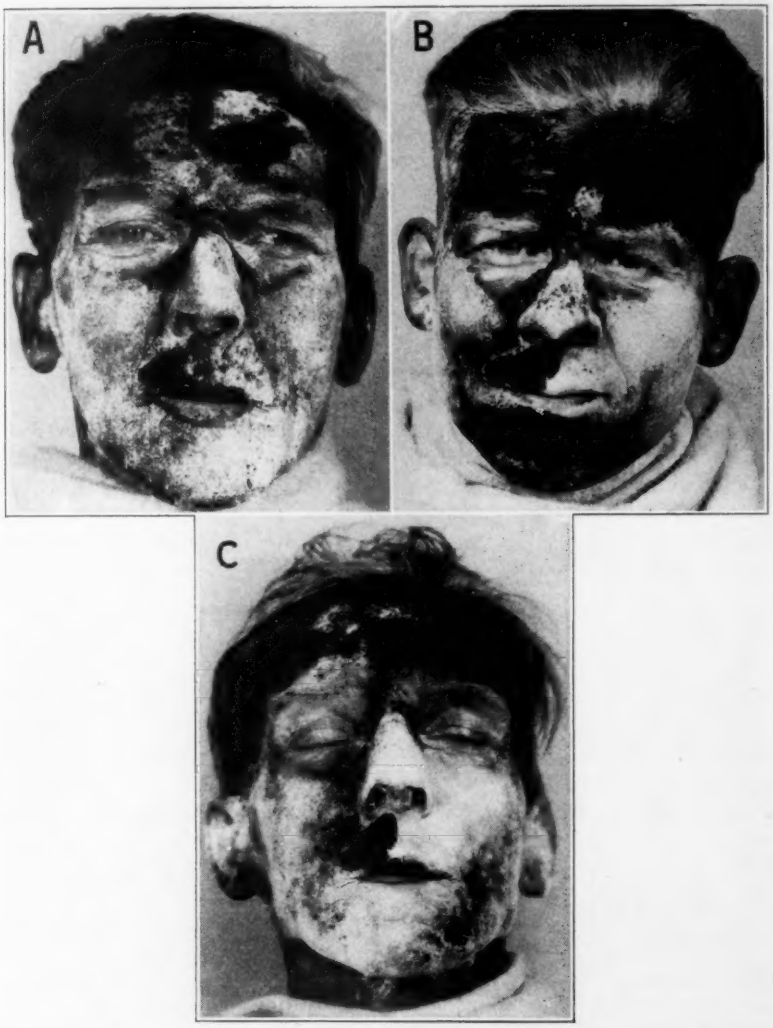

Fig. 4.—Heat sweating. *A* (observation 13), procaine block of the second branch of the left trigeminal nerve in the sphenopalatine fossa; *B* (observation 14), injection of alcohol into the second branch of the left trigeminal nerve near the foramen rotundum, and *C* (observation 15), procaine block of the left infraorbital nerve.

for the first division arise from the internal carotid plexus and enter the ophthalmic branch intracranially (fig. 6). The mild hypohidrosis of the forehead and temple seen after section of the fifth sensory root

may also favor this assumption. On the other hand, most of the sweat fibers for the second and third divisions of the trigeminal nerve join these branches extracranially. They are apparently given off at various levels from the periarterial plexus of the external carotid artery; some, perhaps, may be derived from the deep petrosal nerve and the tympanic

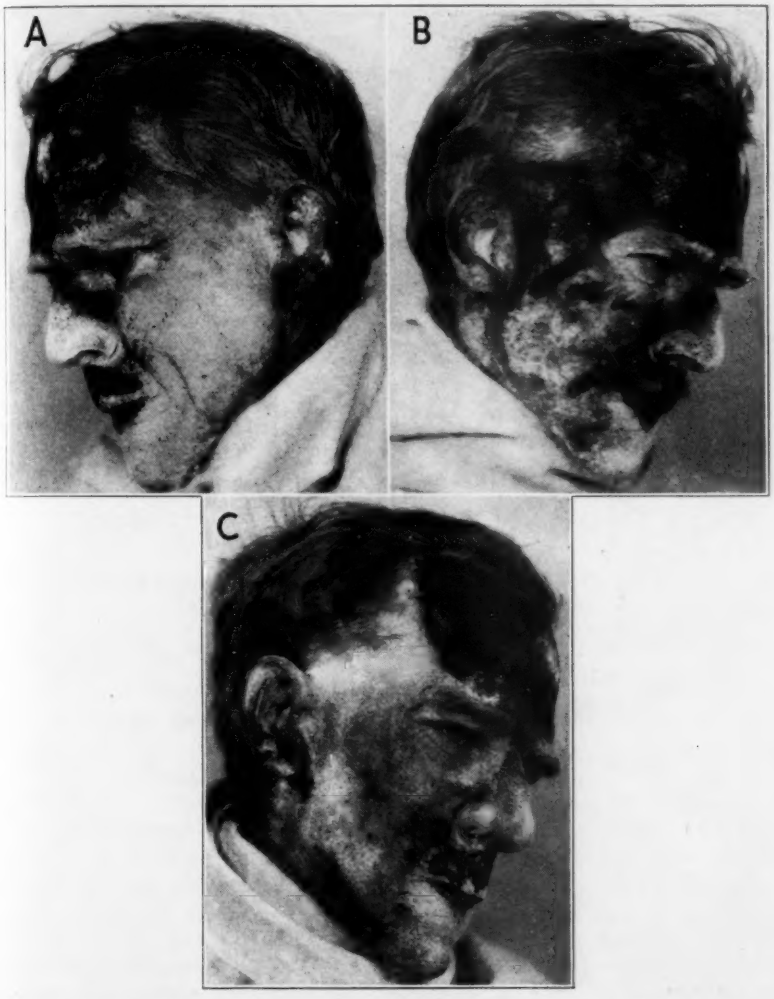

Fig. 5.—Heat sweating. *A* (observation 17), procaine block of the third branch of the left trigeminal nerve at the lingula; *B* (observation 17), the normal side of the face, and *C* (observation 18), procaine block of the right auriculotemporal nerve.

plexus (fig. 6). Apparently, at the base of the skull only a fraction of the sweat fibers are contained in the trigeminal branches, since injection of procaine into the second branch near the foramen rotundum

and into the third branch near the foramen ovale produces complete anesthesia but not complete loss of sweating (in contrast to the complete anhidrosis following the more peripherally placed injections). This statement is not invalidated by cases (such as observation 14) in which an injection of alcohol near the foramen rotundum led to almost complete anhidrosis. In this instance, a large amount of alcohol was injected, with probable overflow into the neighboring areas. Hence, it cannot be ascertained whether only the sympathetic fibers within the second division were paralyzed or those of the adjacent periarterial

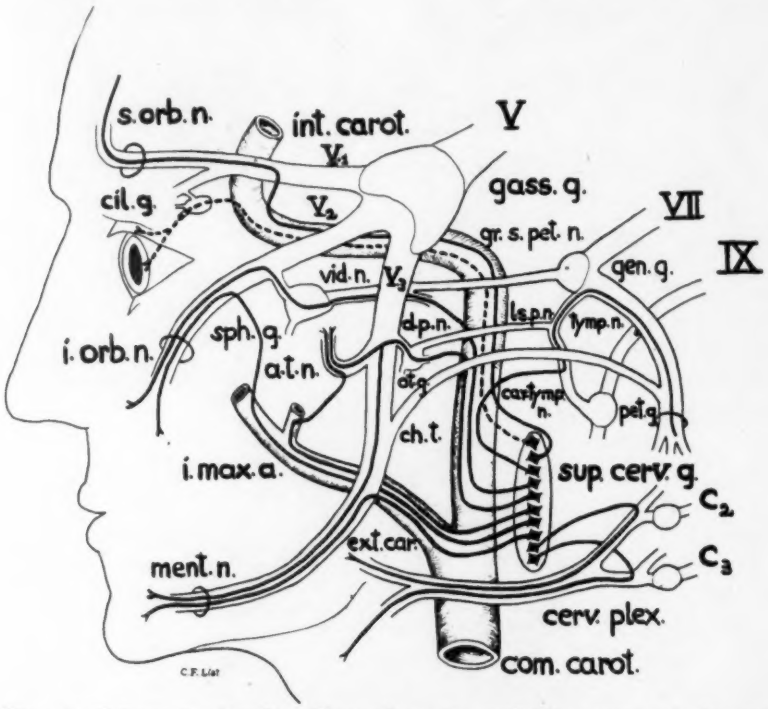

Fig. 6.—Schematic drawing illustrating the probable course of the oculopupillary fibers and of the sympathetic sweat fibers for the face. It is doubtful whether the pathway through the caroticotympanic nerve to the facial nerve carries sweat fibers.

In this figure, *s. orb. n.* indicates the supraorbital nerve; *cil. g,* the ciliary ganglion; *i. orb. n.,* the infraorbital nerve; *sph. g.,* the sphenopalatine ganglion; *ment. n.,* the mental nerve; *a. t. n.,* the auriculotemporal nerve; *ot. g.,* the otic ganglion; *ch. t.,* the chorda tympani nerve; *vid. n.,* the vidian nerve; *gr. s. pet. n.,* the greater superficial petrosal nerve; *l. s. p. n.,* the lesser superficial petrosal nerve; *car. tymp. n.,* the caroticotympanic nerve; *tymp. n.,* the tympanic nerve; *gass. g.,* the gasserian ganglion; *gen. g.,* the geniculate ganglion; *pet. g.,* the petrous ganglion; *sup. cerv. g.,* the superior cervical ganglion; *cerv. plex.,* the cervical plexus; *com. carot.,* the common carotid artery; *int. carot.,* the internal carotid artery; *ext. car.,* the external carotid artery, and *i. max. a.,* the internal maxillary artery.

sympathetic plexus as well. Experiments with injection are conclusive only if small amounts of the anesthetic are injected intraneurally and complete anesthesia is obtained therefrom. For similar reasons, the mild diffuse hypohidrosis mentioned in observation 17 was probably caused by diffusion of the procaine to the sympathetic plexus of the adjacent (internal maxillary) artery.

(*b*) *Lesions of the Seventh and the Chorda Tympani Nerve.*—

Lesion of Intrabulbar Fibers of the Seventh Nerve Root.

OBSERVATION 19 (L. D.).—During the removal of an astrocytoma from the fourth ventricle the right side of the rhomboid fossa was injured. The patient showed complete paralysis of the sixth and seventh nerves on the right, paralysis of lateral gaze to both sides and mild left hemiparesis. The heat test revealed minimal hypohidrosis over the right side of the face.

Lesion of the Intracranial Root of the Extramedullary Portion of the Seventh Nerve.

OBSERVATION 20 (A. C.).—After removal of tumors involving both acoustic nerves, the seventh and eighth nerves on both sides were paralyzed. Heat sweating appeared to be normal and equal on the two sides.

OBSERVATION 21 (R. P.).—The patient suffered from a syphilitic lesion of the right cerebellopontile angle, with almost complete paralysis of the facial nerve. Sweating was equal on the two sides of the face.

Lesion Near the Geniculate Ganglion.

OBSERVATION 22 (J. Z.).—Three days previous to admission paralysis of the right side of the face had occurred. Complete paralysis of the seventh nerve, including the taste, sublingual salivary and lacrimal fibers, was noted on the right side. The sweating test revealed slight hyperhidrosis over the right side of the forehead and nose.

OBSERVATION 23 (H. J.).—Two weeks after an injury to the skull there developed complete paralysis of the right facial nerve, which included the chorda tympani fibers, but secretion of tears was not affected. Slight nerve deafness was present on the right. The sweating test showed definite, though not severe, hyperhidrosis of the right side of the face, particularly on the lateral part of the cheek (fig. 7 *A* and *B*).

Lesion in the Fallopian Canal Distal to the Geniculate Ganglion.

OBSERVATION 24 (A. F.).—Facial palsy had followed a radical operation on the left mastoid. Complete paralysis of the facial nerve, including the chorda tympani fibers, was present on the left side. The sweating test disclosed moderate hypohidrosis over the left side of the face (fig. 7 *C*).

OBSERVATION 25.—Facial palsy had followed an operation on the right mastoid. Complete paralysis of the right facial nerve, including the chorda tympani fibers, was noted. Sweating was normal and equal on the two sides (fig. 7 *D*).

Lesion of the Seventh Nerve Below the Stylomastoid Foramen (Extracranial Portion).

OBSERVATION 26 (W. R.).—After removal of a tumor of the left acoustic nerve, there was complete paralysis of the sixth, seventh and eighth nerves and

paresis of the fifth, ninth and tenth nerves on the left side. The sweating test showed mild hypohidrosis over the left side of the face. Later, the left facial nerve was sectioned below its exit from the stylomastoid foramen and its peripheral end anastomosed with the central end of the spinal accessory nerve. The sweating test, performed five days later, did not reveal any deviation from the findings before operation.

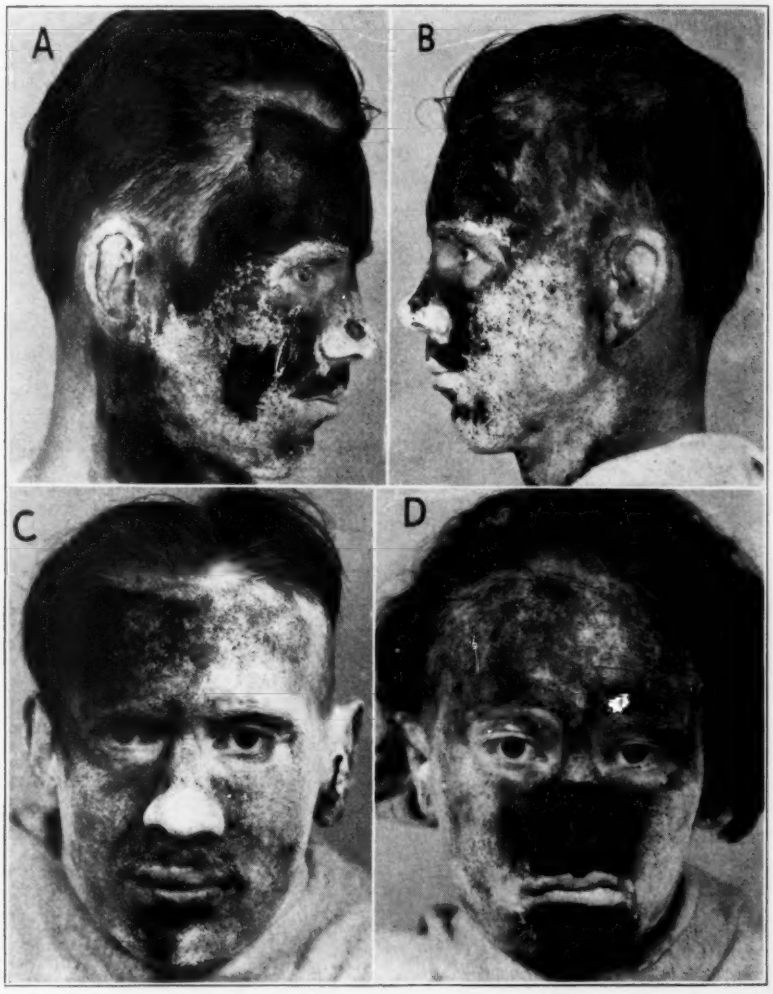

Fig. 7.—Heat sweating. *A* (observation 23), lesion of the right facial nerve near the geniculate ganglion; *B* (observation 23), the normal side of the face; *C* (observation 24), palsy of the left facial nerve following mastoidectomy, and *D* (observation 25), palsy of the right facial nerve following mastoidectomy.

Observation 27 (S. M.).—After extirpation of a tumor of the right parotid gland, complete paralysis of the seventh nerve was noted. Hypesthesia in the distribution of the greater auricular nerve was present. Pulsation of the right tem-

poral artery was not felt. Sweating was equal on the two sides except for slight hypohidrosis over the right temple.

Lesions of the Chorda Tympani Nerve.

OBSERVATION 28 (F. W.).—The left chorda tympani nerve was resected during a radical mastoidectomy. The sweating test showed slight hypohidrosis of the left side of the face, particularly of the forehead.

OBSERVATION 29 (W. S.).—Complete mastoidectomy had been performed several years prior to admission. Two weeks before, a radical operation on the left mastoid, with removal of the chorda tympani nerve, was performed. Complete paralysis of the left and partial paresis of the right chorda tympani nerve were noted. The sweating test demonstrated definite hypohidrosis over the left side of the face, particularly the lateral parts of the cheek, temple and forehead.

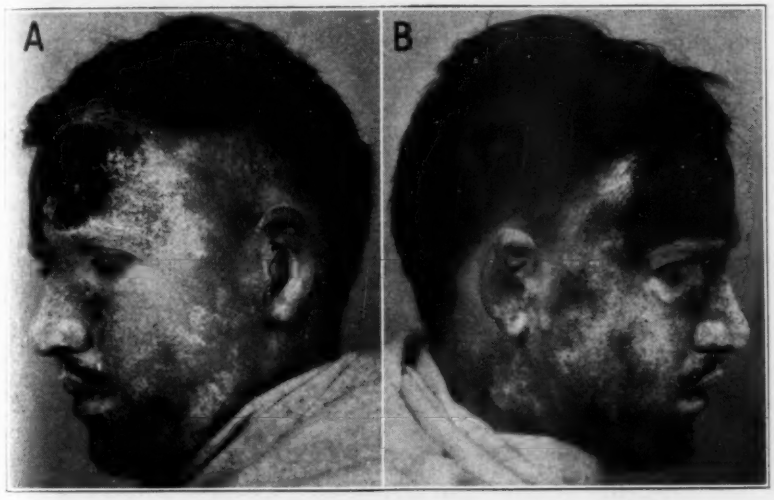

Fig. 8.—Heat sweating. *A* (observation 30), paralysis of the left chorda tympani nerve, and *B* (observation 30), the normal side of the face.

OBSERVATION 30 (E. B.).—Paralysis of the left chorda tympani nerve ensued after radical operation on the left mastoid. Diminution of sweating over the left temple and left side of the forehead could be demonstrated (fig. 8 *A* and *B*).

The observations on sweating responses in 9 cases of lesions of the facial nerve reveal slight or no modification of perspiration. In 2 instances in which the lesion was close to the geniculate ganglion sweating was moderately increased; in 3 other cases in which there were lesions in various locations along the nerve perspiration was equal on the two sides, and in the remaining 4 cases perspiration was slightly decreased on the side of the lesion. In 3 cases of lesion of the chorda tympani nerve with the facial nerve intact there was mild hypohidrosis similar to that seen in some of the cases of facial palsy.

From these experiences, it appears doubtful whether the facial nerve carries any significant number of postganglionic sympathetic sweat fibers. The complete anhidrosis associated with lesions of the peripheral branches of the trigeminal nerve also renders unlikely the existence of the supplementary sympathetic supply from the facial nerve. On the other hand, the lateral parts of the cheek and the parotid area may receive a few sympathetic sweat fibers which enter peripheral branches of the facial nerve through anastomoses with the greater auricular and auriculotemporal nerves. The hypohidrosis encountered in some cases of disease of the middle ear may be due to involvement of the neighboring sympathetic (tympanic and carotid) plexuses. This explanation appears the more probable since these lesions were not sharply circumscribed, but had a widespread inflammatory character. Although it is anatomically possible that sympathetic sweat fibers pass from the caroticotympanic nerves via the tympanic plexus to the facial nerve, no definite clinical proof can be given for such an assumption (see also figure 6). The increased sweating in 2 observations may be due to irritation of the surrounding sympathetic plexus or to stimulation of parasympathetic cholinergic fibers (see later section).

(*c*) *Combined Lesions of the Cranial Nerves.*

OBSERVATION 31 (M. G.).—Section of the sensory root of the right fifth nerve was combined with section of the right major superficial petrosal nerve for relief from trigeminal neuralgia. The sweating test after operation showed minimal hypohidrosis of the right side of the upper lip and the right nasolabial area and temple. Later, the root of the right ninth nerve was sectioned for relief from glossopharyngeal pain, but the result of the sweating test remanied the same (fig. 9 *A*).

OBSERVATION 32 (M. H.).—The patient suffered from a malignant tumor of the right parotid gland, with infiltration of the base of the skull (destruction of bone in the floor of the right middle fossa). There were paralysis of the sixth nerve bilaterally and moderate sensory and motor paresis of the right trigeminal nerve. Complete paralysis of the seventh and the tympani chorda nerves was present on the right, but the secretion of tears was not disturbed. The sweating test revealed complete anhidrosis in the distribution of the second branch of the fifth nerve and hypohidrosis in the area of the first and third branches (fig. 9 *B*).

OBSERVATION 33 (R. C).—The patient had an extensive osteosarcoma of the left side of the maxilla. After section of the left supraorbital and infraorbital nerves, radical resection of the tumor was performed, followed by high voltage roentgen therapy. The left side of the face showed a huge area of destruction: The left side of the nose, the left orbital contents, the left side of the maxilla and the contents of the left pterygopalatine fossa were completely removed. Anesthesia was noted in the area of the left supraorbital nerve and over the left side of the upper lip. There was complete paralysis of the frontal and middle branches of the left facial nerve, but the lower branch was not involved. Subsequent section of the sensory roots of the fifth and ninth nerves on the left (suboccipital approach) was performed for relief from pain. The sweating test after operation showed anhidrosis in the distribution of the supraorbital nerve and in the

remaining cutaneous area of the infraorbital nerve; otherwise, no change was noted (fig. 9 *C;* see also observation 9).

Intracranial section of the ninth nerve does not modify the heat sweating of the face. It is also doubtful whether section of the fifth

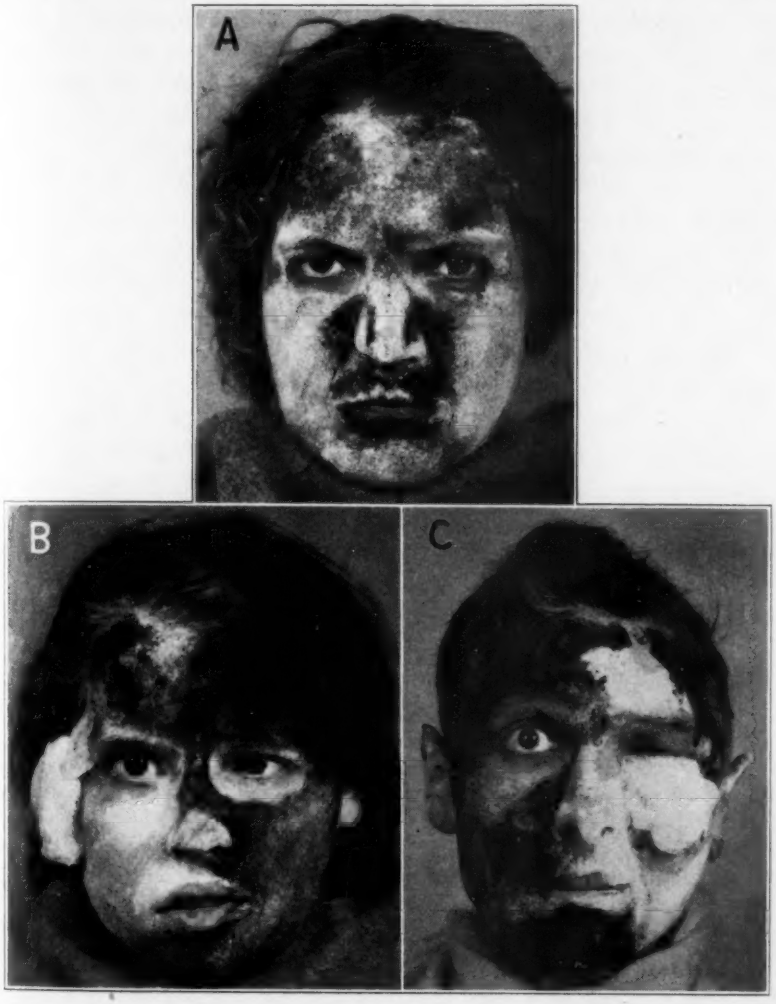

Fig. 9.—Heat sweating. *A* (observation 31), section of the sensory root of the right trigeminus, right major superficial petrosal and right ninth nerves; *B* (observation 32), malignant tumor of the parotid gland with infiltration of the base of the skull and multiple cranial nerve palsies, and *C* (observation 33), osteosarcoma of the left side of the maxilla, with multiple cranial nerve palsies, partially produced by surgical section. For details for *B* and *C*, see the text.

sensory root plus that of the major superficial petrosal nerve account for the slight hypohidrosis, because it is not more marked than that seen in association with section of the sensory root alone.

Observation 33, in which there were multiple nerve lesions, is particularly instructive, since the sweating remained normal in the distribution of the third branch of the fifth nerve (mental and auriculotemporal nerves). When multiple cranial nerve palsies are present a discrepancy between the changes in sensation and those in sweating may be important for localization. In observations 9 and 33 the sweating test clearly demonstrated lesions of the peripheral branches of the trigeminal nerve in spite of the coexisting section of the sensory root. In case 32 the contrast between the complete anhidrosis and the partial loss of sensation in the area of the second division of the nerve suggests a severe lesion of the cranial sympathetic plexus before its junction with the peripheral portion of the second branch.

SWEATING RESPONSES OF CHOLINERGIC (PARASYMPATHETIC) NATURE

SWEATING RESPONSE FOLLOWING INJECTION OF PILOCARPINE (LIST AND PEET [4])

After complete degeneration of postganglionic cervical sympathetic sweat fibers secretion of the sweat glands of the face can still be elicited by parasympathomimetic drugs, such as pilocarpine or mecholyl. Langley, Burn and Wilson explained this phenomenon by the assumption that the drugs act directly on the sweat glands. Other authors (Foerster and Guttmann and List [5]) considered the preservation of pilocarpine sweating after cervical sympathetic ganglionectomy as evidence for double innervation of the sweat glands of the face. A few observations from a separate study dealing with the sweating responses following injection of pilocarpine follow.

Observation 34 (R. J.) (See also observation 1).—One year previously the right superior cervical ganglion had been removed. Pilocarpine produced sweating of the face bilaterally, but a diminished response on the right side.

Observation 35 (P. L.) (See also observation 11).—Both supraorbital nerves were severed by an injury to the head producing compound fracture of the frontal bone. The pilocarpine test, performed sixteen days after the injury, produced no sweating in the anesthetic area.

Observation 36 (F. F.) (See also observation 10).—Procaine block of the left supraorbital nerve produced complete anesthesia in the area supplied by this nerve. Pilocarpine elicited approximately an equal distribution of sweating over the forehead, except for some diminution at the site of injection.

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4. List, C. F.: Studies of Sweat Secretion in Man, Univ. Hosp. Bull., Ann Arbor **2**:27-28, 1936. List and Peet.[1]

5. Guttmann, L., and List, C. F.: Zur Topik und Pathophysiologie der Schweiss-sekretion, Ztschr. f. d. ges. Neurol. u. Psychiat. **116**:504-536, 1928. Guttmann, L.: Schweiss-sekretion des Menschen in ihren Beziehungen zum Nervensystem, ibid. **135**:1-47, 1931.

Even after long-standing complete degeneration of the postganglionic cervical sympathetic sweat fibers, the sweating response to pilocarpine in the affected area was diminished only. After section of the supraorbital nerve, however, pilocarpine sweating was completely lost as soon as the nerve fibers had degenerated (two weeks). It was too early for the sweat glands to have undergone any anatomic change. Consequently, it must be assumed that (1) in customary doses pilocarpine acts mainly on the nerve fibers supplying the sweat glands rather than on the sweat glands themselves and (2) the peripheral nerves (e. g., the supraorbital nerve) carry fibers susceptible to pilocarpine which are not contained in the cervical sympathetic outflow. Although injection of procaine hydrochloride into the supraorbital nerve produces complete functional block of all nerve fibers, it fails to reduce materially the pilocarpine sweating. This drug, therefore, must be considered to act at a point distal to the nerve block, i. e., in all probability, on the nerve endings.

According to the terminology of Dale,[6] nerve fibers which are stimulated by pilocarpine and derivatives of choline but are paralyzed by atropine are designated as cholinergic fibers. Most of the cranial nerves contain such cholinergic fibers. All the parasympathetic secretory fibers which pass through the nervus intermedius (Babkin, Gibbs and Wolff [7] and Gibbs and Szelöczey [8]) and the glossopharyngeal and vagus nerves belong to this group. Furthermore, all the vasodilator fibers (in the trigeminus nerve, for instance) have cholinergic properties. It is readily seen, therefore, that pilocarpine is able to evoke lacrimation, salivation and vasodilation. It is not easy to understand why this parasympathomimetic drug should produce sweating, since the sweat glands are known to be directly supplied by postganglionic sympathetic fibers only. To overcome this discrepancy, Dale and Feldberg [9] assumed that the sweat fibers, although anatomically of sympathetic (thoracolumbar) origin, possess the physiologic and pharmacologic properties of cholinergic (parasympathetic) fibers. This theory is corroborated both by animal experimentation and by clinical observations. The slight diminution in pilocarpine perspiration on the side of operation following cervical

6. Dale, H. H.: Progress in Autopharmacology: II. Acetylcholine: Its Natural Occurrence and Probable Function, Bull. Johns Hopkins Hosp. **53**:312-329, 1933.

7. Babkin, B. P.; Gibbs, O. S., and Wolff, H. G.: Die humorale Uebertragung der Chorda tympani-Reizung, Arch. f. exper. Path. u. Pharmakol. **168**:32-37, 1932.

8. Gibbs, O. S., and Szelöczey, J.: Die humorale Uebertragung der Chorda tympani-Reizung, Arch. f. exper. Path. u. Pharmakol. **168**:64-88, 1932.

9. Dale, H. H., and Feldberg, W.: The Chemical Transmission of Secretory Impulses to the Sweat Glands of the Cat, J. Physiol. **82**:121-127, 1934.

ganglionectomy suggests that this hypohidrosis may be due to degeneration of some postganglionic sympathetic fibers with cholinergic properties. On the other hand, the complete anhidrosis produced by pilocarpine after section of the peripheral branches of the trigeminal nerve can be explained only by the assumption that the peripheral branches of this nerve carry an additional set of cholinergic fibers, which do not arise from the sympathetic thoracolumbar system. The only trigeminal cholinergic fibers supplying the skin are the vasodilator fibers, but, according to present knowledge, they do not make direct contact with the sweat glands. How, then, do these vasodilator fibers influence the sweating, and what is the probable mechanism of such an action? Again, the work of Dale and his collaborators gives a plausible explanation, which is now confirmed by experiments on animals. Stimulation of cholinergic fibers liberates at the nerve endings a substance with properties resembling those of acetylcholine. This chemical intermediary transmits the nerve impulse to the end organs. Whenever vasodilator fibers are stimulated by pilocarpine, the acetylcholine-like body is set free in the skin and may leak from the arterioles and capillaries to the cells of the neighboring sweat glands. Thus, sweat may be secreted by indirect chemical stimulation of the gland cells. Since after complete degeneration of peripheral nerves all cholinergic parasympathetic and postganglionic sympathetic fibers are destroyed, this mechanism no longer works, and the injection of pilocarpine fails to evoke perspiration. On the other hand, degeneration of the postganglionic sympathetic fibers alone does not interfere with the cholinergic supply by the cranial parasympathetic nerves.

It has been known that sympathectomized (deefferented) end organs become sensitized to the direct action of substances such as epinephrine and acetylcholine. When the acetylcholine-like transmitter is liberated by stimulation of cholinergic fibers, the response of the deefferented (sympathectomized) sweat glands may become hyperactive. This sensitization to acetylcholine is illustrated by the following observations.

OBSERVATION 37 (H. C. K.).—The patient exhibited a lesion of the right superior cervical ganglion. Complete anhidrosis of the right side of the face was demonstrated by the heat sweating test (fig. 10 *A*). Pilocarpine produced at first hyperhidrosis over the right deefferented side (fig. 10 *B*); in the later stages of the test the sweating became increasingly pronounced over the healthy left side (fig. 10 *C*).

The initial phase of hyperhidrosis is due to sensitization of the deefferented sweat glands to the acetylcholine liberated by stimulation of the cholinergic fibers.

In the second stage the perspiration of the sympathectomized side lags behind that of the normal side because the function of the cholinergic fibers contained in the cervical portion of the sympathetic chain is abolished and only the parasympathetic cholinergic fibers remain active.

SO-CALLED GUSTATORY SWEATING

Pilocarpine sweating illustrates the effect of stimulation of cholinergic nerve fibers by pharmacodynamic means. A similar sweating response may be obtained by purely neurodynamic excitation. This is exemplified by the so-called gustatory sweating response.

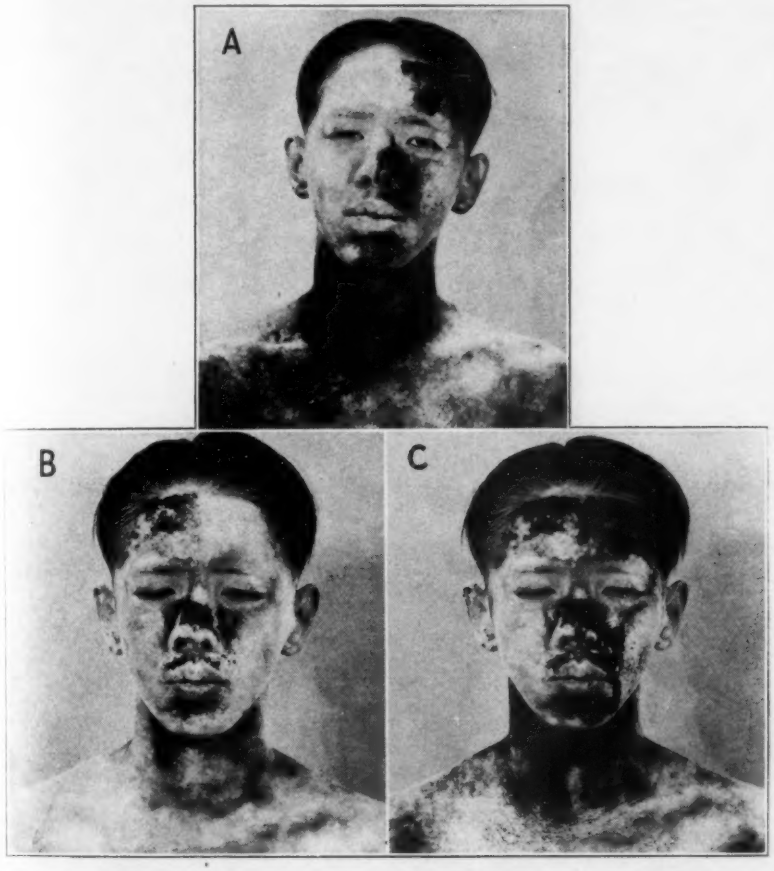

Fig. 10 (observation 37).—Lesion of the right superior cervical sympathetic ganglion. *A*, heat sweating; *B*, initial stage of pilocarpine sweating, and *C*, late stage of pilocarpine sweating.

In many normal persons chewing and tasting spicy food produce sweating over the lips, nose and nasolabial folds. This "gustatory perspiration" is slight under physiologic conditions, but after degeneration of the postganglionic sympathetic sweat fibers the response may be increased. The following 2 cases illustrate the physiologic mechanism involved in gustatory perspiration.

OBSERVATION 38.[10]—The patient stated that he perspired on the left side of the face whenever he ate sour food. The heat sweating test showed complete anhidrosis of the left side of the face and neck (fig. 11 *A*).

Gustatory Sweating Test.—Immediately after tasting vinegar perspiration appeared over the entire left side of the face (fig. 11 *B*). The sweating response

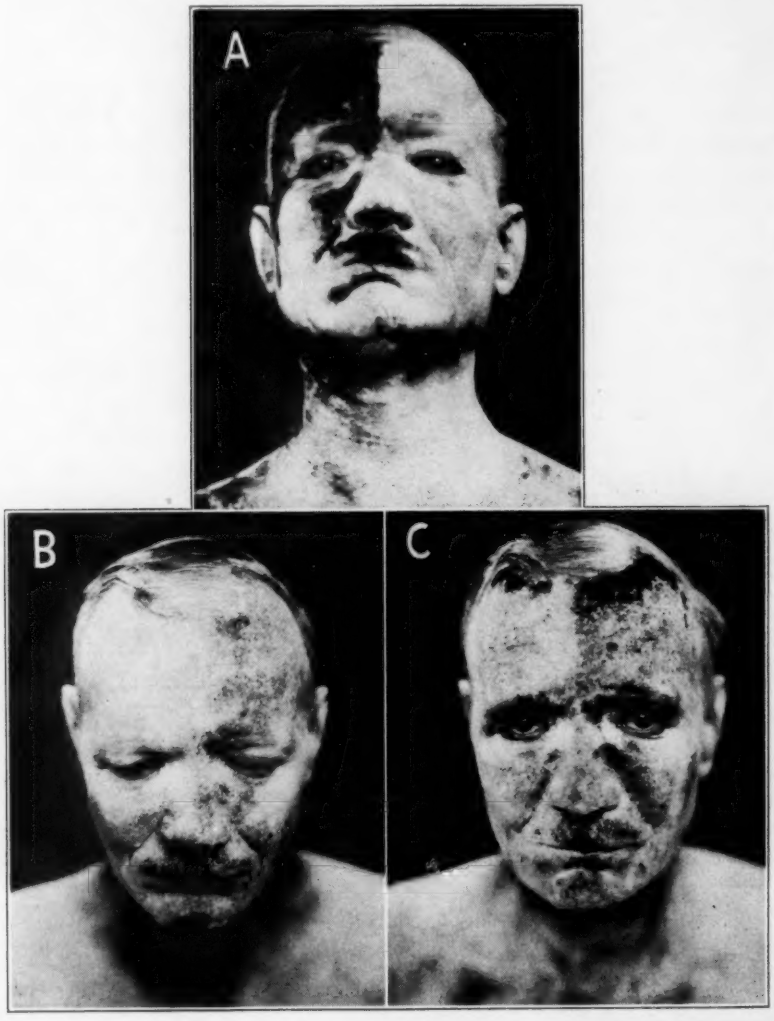

Fig. 11 (observation 38).—Probable lesion of the cervical portion of the left sympathetic chain. *A*, heat sweating; *B*, gustatory sweating, and *C*, initial stage of pilocarpine sweating.

increased each time immediately after taking a sip of vinegar. At another test a cotton swab soaked with vinegar was applied successively to the tip of the

10. This case has been reported previously by Guttmann and List.[5]

tongue, the base of the tongue and the posterior wall of the pharynx. The outbreak of sweating was strongest when the vinegar was brought in contact with the base of the tongue.

Injection of pilocarpine produced sweating which in the initial stage was limited to the left side of the face (fig. 11 *C*); later, the perspiration of the left side lagged considerably behind that of the normal right side (compare with observation 37).

OBSERVATION 39 (R. J.).—(See observation 1.) A year before this observation, the patient had had a right superior cervical ganglionectomy. Since that time he had experienced sudden sharp pains radiating from the region of the right temporomandibular joint to the temple whenever he started to eat. This was followed by an outbreak of sweat, while the pain subsided. Heat sweating was completely abolished over the right half of the face (fig. 1 *A*). After eating a spicy sandwich he immediately complained of the aforementioned pain. Soon,

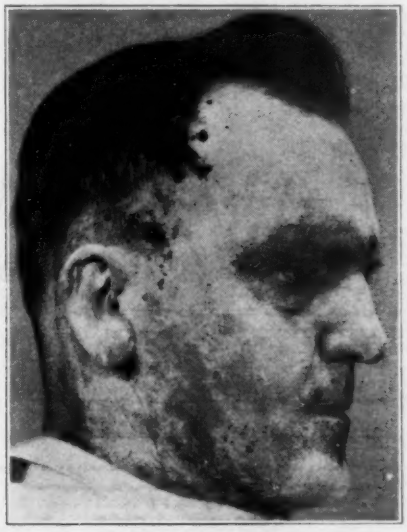

Fig. 12 (observation 39).—Gustatory sweating following resection of the right superior cervical sympathetic ganglion (see observation 1).

mild perspiration became visible over the right half of the nose and upper lip, but much more conspicuous blotches of moisture appeared over the right temple (fig. 12).

The immediate outbreak of perspiration after application of a gustatory stimulus proves that the reaction is of a reflex nature and not the result of a pharmacodynamic effect (Guttmann and List [5]). The afferent arc of the gustatory sweating reflex is formed chiefly by the gustatory fibers of the ninth nerve, but it is likely that the taste fibers of the chorda tympani (intermedius) nerve also participate. The afferent path of the reflex must be represented bilaterally, since it is not abolished by cocainization of the ipsilateral half of the tongue (Uprus, Gaylor

and Carmichael [11]). Even cocainization of the entire tongue does not entirely suppress the phenomenon, since receptive areas of the soft palate (innervated by the ninth nerve) remain intact (Fridberg [12]). Simple mechanical stimulation of the tongue or mastication of tasteless objects elicits no sweating response; hence, the exteroceptive and proprioceptive sensory fibers of the fifth nerve play no role in the afferent mechanism. Rappoport [13] and we (unpublished data) observed patients who exhibited gustatory sweating when they merely looked at spicy food. Here, then, the direct excitation of gustatory fibers was substituted by visual perception leading to a psychic gustatory association. The various modes of stimulation have one effect in common; namely, they all evoke salivation. It is likely therefore that the efferent mechanism of gustatory perspiration is linked to the process of salivation. The salivary glands receive innervation from the auriculotemporal nerve (fibers of the ninth nerve) and from the chorda tympani nerve (fibers of the intermedius nerve). That the salivary nerves have an active part in, or are even identical with, the effector mechanism was conclusively shown by Uprus, Gaylor and Carmichael.[11] In their case a localized submental sweating response was abolished by injection of procaine hydrochloride into the ipsilateral lingual nerve distal to the entrance of the chorda tympani nerve.

How can the relationship between salivation and sweating be explained? Salivation is elicited by the combined action of secretory and vasodilator impulses, which constitute the functions of cholinergic nerve fibers. Thus, reflex salivation following gustatory stimulation implies a powerful excitation of cranial cholinergic (parasympathetic) fibers, with the consequent liberation of the chemical transmitter at the nerve endings. This substance with the properties of acetylcholine is capable of producing not only salivary secretion and vasodilation but also (apparently by diffusion) slight sweating of the face. Factually, the physiologic mechanisms of gustatory and those of pilocarpine sweating are similar. However, in the first case the phenomenon is localized and is brought into play by a purely neurodynamic stimulus; in the second, the reaction is generalized and is produced by pharmacodynamic stimulation.

After degeneration of the postganglionic sympathetic fibers (following superior cervical ganglionectomy) gustatory, like pilocarpine, sweating is increased over the deefferented areas of the face. This overactive response is probably caused by sensitization of the deefferented sweat

11. Uprus, V.; Gaylor, J. B., and Carmichael, E. A.: Localized Abnormal Flushing and Sweating on Eating, Brain **57**:443-453, 1934.

12. Fridberg, D.: Das auriculotemporale Syndrom, Deutsche Ztschr. f. Nervenh. **121**:225-239, 1931.

13. Rappoport, M., cited by Fridberg.[12]

glands to the acetylcholine released by stimulation of the cholinergic cranial parasympathetic fibers.

Gustatory sweating may show a uniform increase over the entire sympathectomized side of the face (observation 38) or more circumscribed exaggeration of sweating (observation 39). Localized gustatory hyperhidrosis may be the result of regional sympathetic paralysis, such as was present in the case reported by Uprus, Gaylor and Carmichael.[11] Here, the gustatory perspiration occurred over the left submental area, which was shown not to have a proper sympathetic control (demonstrated by tests for cutaneous temperature only; heat sweating tests were not done).

Still another type of localized gustatory hyperhidrosis is known in the literature as the "auriculotemporal syndrome [11] (Frey,[14] Fridberg,[12] Kaminsky,[15] Needles,[16] Rappaport [13] and Thomas [17]) because it occurs in the distribution of the auriculotemporal nerve and its anastomotic branches with the facial nerve (Frohse's nerve). Two cases illustrate this syndrome.

OBSERVATION 40.—Several months previously S. M. underwent removal of a tumor of the right parotid gland, which was followed by paralysis of the right facial nerve. He complained of pains and sweating in the right temple while eating. Examination revealed a scar along the ascending right ramus of the lower jaw. Almost complete paralysis of the right facial nerve, of peripheral type, was present, but a few synkinetic movements were seen in the triangularis and quadratus labii inferioris muscles during chewing. Slight hypesthesia was found in the area of the greater auricular nerve (as far as it was severed by the incision), and an area of cutaneous hyperalgesia was mapped out over the lateral part of the cheek, temple, ear and retroauricular area. The heat test showed slight and poorly demarcated hypohidrosis over the right temple and lateral parts of the right cheek (fig. 13 *A*). Eating spicy food immediately produced a painful burning sensation in front of the right ear and temple, followed by profuse sweating in the distribution of the auriculotemporal nerve (fig. 13 *B*).

OBSERVATION 41.—Forty-eight years ago I. T. suffered from an abscess of the left parotid gland, which healed after incision. Since that time eating has produced blushing and sweating of the left cheek and temple. Examination showed complete atrophy of the left parotid gland. The skin overlying the parotid area was tightly adherent to the masseter muscle; it was atrophic and glossy and contained many tiny telangiectases. There was no gross scar, however. Mild facial paresis

14. Frey, L.: Le syndrome du nerf auriculotemporal, Rev. neurol. **2**:97-104, 1923.

15. Kaminsky, S. D.: Das "auriculo-temporale (Parotitis) Syndrom" bei Syringomyelie, Deutsche Ztschr. f. Nervenh. **109**:296-309, 1929.

16. Needles, W.: The Auriculotemporal Syndrome, Arch. Neurol. & Psychiat. **35**:357-360 (Feb.) 1936.

17. Thomas, A.: Le double réflexe vaso-dilatateur et sudoral de la face consécutif aux blessures, de la loge parotidienne; les pararéflexes, Rev. neurol. **1**:447-460, 1927.

was present, with marked contracture and occasional ticlike twitchings. Slight hyperalgesia was noted over the left parotid region and lateral part of the left cheek, without sharp demarcation. The heat sweating test showed slight hypohidrosis of the left temple. Eating a spicy sandwich within a few seconds produced vasodilation in front of the left ear and over the left cheek (fig. 13*C*). Shortly thereafter, profuse perspiration appeared over the left auriculotemporal area and, to a much lesser degree, in the region of the preceding malar vasodilatation (fig. 13*D*). Studies on the temperature of the skin showed a rise in temperature of from 1.3 to 1.6 degrees C. (2.3 to 2.8 degrees F.) in the malar area of vasodilata-

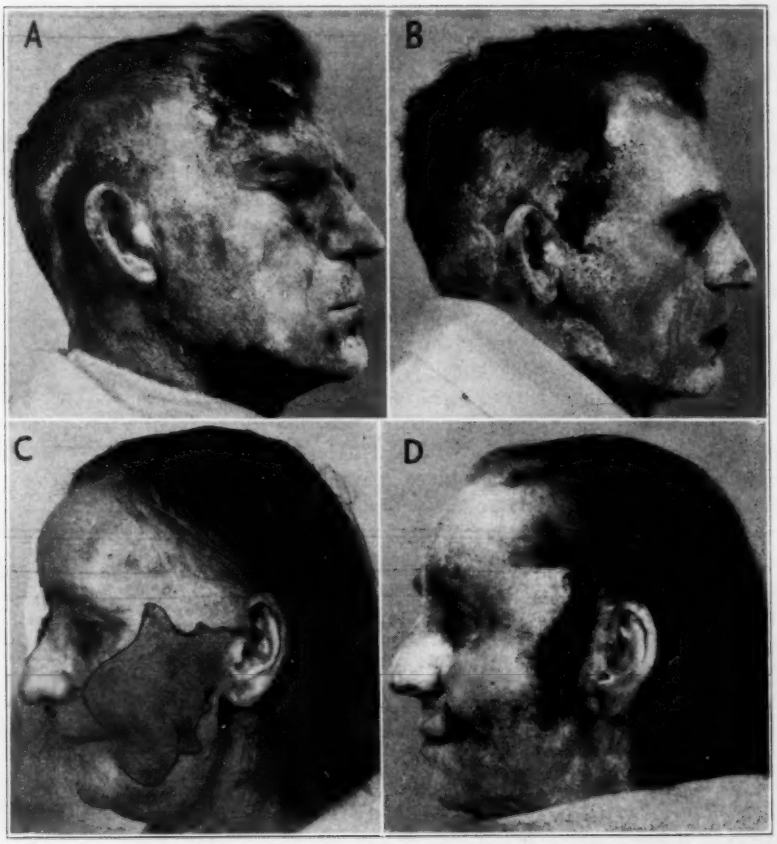

Fig. 13.—*A* (observation 40), heat sweating in a case of right auriculotemporal syndrome following removal of a tumor of the parotid gland; *B* (observation 40), gustatory sweating; *C* (observation 41), area of vasodilatation after eating in a case of left auriculotemporal syndrome following abscess of the parotid gland, and *D* (observation 41), gustatory sweating.

tion, whereas it dropped 1.2 C. (2 degrees F.) in the profusely perspiring temporal region.

The typical auriculotemporal syndrome consists of pain (or hyperesthesia), vasodilatation and sweating in the distribution of the auriculo-

temporal nerve during eating. Pain and vasodilatation precede the sweating. The area of vasodilatation and that of sweating may not be identical (observation 41 [18]). Vasodilatation and sweating are undoubtedly caused by reflex stimulation of cholinergic fibers in the auriculotemporal nerve. Although the facial nerve is found to be involved in most cases, its lesion per se is not responsible for the phenomena described except that it may imply involvement of the anastomotic branches of the auriculotemporal nerve (Frohse's nerve), as in observation 41. The slightly diminished heat sweating in the last 2 cases and in several observations reported in the literature suggests that there is some loss of postganglionic sympathetic innervation.

The diminution of heat sweating, however, is so slight that one can hardly explain the excessive gustatory perspiration merely by sensitization of deefferented sweat glands.

The typical auriculotemporal syndrome usually occurs after trauma to the parotid area or severe parotitis. As a rule, it appears at a considerable period after the primary lesion has healed with extensive scar formation. It had been surmised that a sclerotic parotid gland cannot properly expand when secreting and exerts mechanical pressure on the intraglandular auriculotemporal nerve plexus, with the resultant sweating (Needles [16]). This explanation does not do justice to cases in which the glandular structures were completely destroyed. Another hypothesis assumes that in the process of regeneration nerve fibers destined for the salivary glands form abnormal connections with cutaneous sympathetic fibers for the sweat glands (Ford [19]). The formation of such a nerve anastomosis is theoretically possible, but is unlikely. A third theory, which we favor, assumes that the scars in the parotid gland, and perhaps attempts at regeneration in the strangulated twigs of the auriculotemporal nerve, maintain a local condition of abnormal irritability in the cholinergic fibers. Whichever explanation is correct, the typical auriculotemporal syndrome appears to be caused by pathologic irritability of cholinergic fibers rather than by sensitization of deefferented sweat glands.

SUMMARY

The sweating responses of the face were studied with Minor's iodine and starch method in patients presenting nerve lesions.

The distribution of the sympathetic sweat fibers was determined by the thermoregulatory sweating test. The postganglionic sweat fibers arising in the superior cervical ganglion either pass through the periarterial plexus of the external carotid artery or are carried into the

18. We have recently seen a case in which flushing, but no sweating, was present.

19. Ford, F. R.: Paroxysmal Lacrimation During Eating as a Sequel of Facial Palsy, Arch. Neurol. & Psychiat. **29**:1279-1288 (June) 1933.

cranium via the periarterial plexus of the internal carotid artery (internal carotid nerve). The trigeminus nerve receives its sweat fibers distal to the gasserian ganglion. Most of the fibers for the ophthalmic branch probably enter this nerve intracranially, whereas the fibers destined for the second and third divisions join these nerves extracranially. The peripheral branches of the fifth nerve contain all sweat fibers for the trigeminal area.

There is no definite proof that the facial nerve carries sympathetic sweat fibers, except perhaps a few for the auriculotemporal and parotid areas (anastomotic branches from the auriculotemporal and greater auricular nerves). The intracranial portions of the glossopharyngeal, the greater superficial petrosal and the chorda tympani nerves contain no sympathetic sweat fibers.

Perspiration of the face is produced also by stimulation of so-called cholinergic fibers which act indirectly by releasing a chemical transmitter, probably acetylcholine. Not only various parasympathetic nerves (fifth, seventh, ninth and tenth) but some of the postganglionic fibers of the cervical portion of the sympathetic chain have cholinergic properties. A "cholinergic sweating" response can be elicited in two ways: 1. A generalized response of the entire body follows administration of parasympathomimetic drugs, such as pilocarpine or mecholyl. 2. A neurodynamic response, confined to the face, is produced by the gustatory salivary reflex.

After degeneration of a peripheral branch of the trigeminal nerve cholinergic, like thermoregulatory, sweating is abolished in the distribution of this nerve. After postganglionic sympathetic denervation (superior cervical ganglionectomy) the cholinergic response may be diminished, or it may be increased because the deefferented sweat glands become sensitized to acetylcholine.

Gustatory sweating depends on the reflex stimulation of cranial cholinergic fibers. A faint gustatory sweating response is present in many normal persons. Pathologic gustatory hyperhidrosis occurs: (1) in sympathectomized areas, probably owing to sensitization to acetylcholine, and (2) as the auriculotemporal syndrome, which is explained by abnormal local irritability of cholinergic fibers.

DISCUSSION

DR. WILDER PENFIELD, Montreal, Canada: This demonstration of increased sensitivity of the sweat glands to the influence of acetylcholine is interesting. The phenomenon is anologous to the demonstration by James White that after sympathectomy there is a tenfold increase in sensitivity of the peripheral vessels to the influence of epinephrine. This sensitivity is greater if the postganglionic, and not the preganglionic, neuron is removed. I should like to ask

Dr. List whether this increased sensitivity to the influence of acetylcholine occurs if the preganglionic cells are removed or whether it develops only after removal of the postganglionic neuron.

Dr. Abraham Myerson, Boston: A possible explanation of some of the phenomena may be found in the facts reported by Drs. List and Peet. My associates and I have carried on a considerable number of experiments on sweating. Sweating seems to be a cholinergic phenomenon, whether the sweat glands are innervated by the sympathetic system or not. We believe that the sympathetic system can manufacture acetylcholine at its terminal neuron, just as it does at the ganglionic neuron. The proof lies in the following: First, all the cholinergic drugs, such as acetylcholine and mecholyl, produce sweating. None of the adrenergic drugs, such as benzedrine, epinephrine or ephedrine, do so. Furthermore, if acetylcholine or mecholyl is injected intradermally local sweating takes place. This local sweating, like every other cholinergic function, can be blocked by atropine and enhanced by prostigmin (the dimethylcarbamic ester of 3-hydroxyphenyltrimethylammonium methyl sulfate). Furthermore, it is not all affected by epinephrine, benzedrine or ephedrine.

From our pharmacologic work on sweating, it seems that the sympathetic nervous system is a mediator of cholinergic activity, at any rate as far as sweating is concerned.

That sweating is increased when the sympathetic influence is removed falls in line with many experiments which show that the tissues themselves react more effectively to drugs of the cholinergic type if the sympathetic or the parasympathetic fibers are removed. For example, Cannon has shown that cholinergic stimulation of the intestine after it has been denervated is far more effective than when the nervous system is intact. In other words, the nervous system is not so much a stimulator of these reacting cells as a regulator of their activity. If acetylcholine is injected into the denervated part of the skin one obtains a good sweating reaction. In fact, one gets a better sweating reaction than if the nervous system is intact. I do not believe that the thesis of the necessity of special cholinergic fibers can be proved. The secretion of sweat is a cholinergic phenomenon, regardless of its innervation by the sympathetic nervous system.

Dr. M. M. Peet: The sweating tests which Dr. List has presented are of definite value to the neurosurgeon. These tests demonstrate graphically any impairment of the cutaneous sympathetic nerve supply, no matter of what origin. They are thus at times of considerable localizing value. These sweating tests also provide definite postoperative information as to the extent and completeness of sympathectomy.

Dr. C. F. List: I should like to answer Dr. Penfield's question first. Sweating of the face as a result of the injection of pilocarpine usually is increased for the first three weeks after postganglionic, as well as preganglionic, denervation. With time, however, there are slight diminution of the sweating in the cases of preganglionic denervation and marked hypohidrosis in those of postganglionic denervation. The sensitization to acetylcholine of the sweat glands which have been deprived of their postganglionic nerve supply may be recognized in some cases by an initial stage of hyperhidrosis of the sympathectomized area whereas in the later stages of the sweating test the perspiration is diminished on the denervated side.

As to Dr. Myerson's remark: We have found evidence that parasympathomimetic drugs, such as pilocarpine or mecholyl, act mainly on cholinergic nerve

endings rather than on the sweat glands themselves. Subcutaneous injections of customary doses of pilocarpine (or mecholyl) fail to evoke visible sweating in cases of degeneration of perpiheral nerves of short duration (such as occurs from two to three weeks after section of the supraorbital nerve). If only a few weeks have elapsed after the operation, the sweat glands themselves are still intact whereas the nerves have degenerated. In such a case the amount of the drug available to the denervated sweat glands is insufficient to produce visible perspiration. Therefore, normal pilocarpine sweating must depend on an intact nerve supply. I shall not deny that sweating could be produced even in cases of degeneration of peripheral nerves if the concentration of the drug in the skin could be made high enough. This is not possible, however, in man because of the generalized reactions following subcutaneous injection of these drugs.

Pilocarpine and mecholyl excite the cholinergic fibers in the peripheral nerves and by stimulation of these fibers liberate enough acetylcholine to induce sweating. The cholinergic nerve fibers, therefore, represent the necessary "starter" or amplifier mechanism for pilocarpine or mecholyl sweating. We have had no personal experiences with intracutaneous injection of parasympathomimetic drugs.

QUANTITATIVE OLFACTORY TESTS

VALUE IN LOCALIZATION AND DIAGNOSIS OF TUMORS OF THE BRAIN, WITH ANALYSIS OF RESULTS IN THREE HUNDRED PATIENTS

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AND

JANE STEWART

NEW YORK

Our aim in this study of our experiences with the olfactory tests employing the blast injection and stream injection of odors was twofold. We desired to learn whether a larger experience would confirm the belief that the quantitative olfactory tests are of value for the localization of tumors of the brain and whether the tests have value for diagnosis as well as for localization.

The tests were made on 150 patients with tumor of the brain verified by operation, encephalographic or ventriculographic examination or autopsy and on 150 patients who were suffering from an intracranial condition other than tumor.

The conditions included:

Tumors—	No. of Patients
Frontal or subfrontal region	51
Pituitary gland	32
Temporal region	7
Parietal and occipital regions	14
Parasagittal region	9
Corpus callosum	4
Bucconeural pouch	2
One cerebral hemisphere	14
Subtentorial region	17
	150
Other Diseases and Disorders—	
Convulsive seizures	54
Encephalitis	16
Vascular lesions	5
Multiple sclerosis	12
Headaches of unknown cause	12

From the Clinical Research Laboratories of the Neurological Institute of New York.

Supported by a grant for research on tumors of the brain from the John and Mary R. Markle Foundation.

Serous meningitis	6
Paralysis agitans	3
Cerebrospinal syphilis	11
Various lesions	31
	150

PRINCIPLE ON WHICH OLFACTORY TESTS ARE BASED AND ODORS USED IN TESTS

Ordinarily, odors cannot be recognized unless they are inhaled. No matter how volatile the odorous substance, held under the nostrils or actually introduced into the opening of the nasal passages, its odor cannot be recognized unless it is carried to the olfactory membrane with the current of air which is inhaled during breathing or sniffing. This indicates that odors can adequately stimulate the olfactory receptors only when a stream of air carrying the odor impinges on the olfactory membrane with a certain degree of force.

Investigations made by one of us showed that odors can be recognized without breathing if the air and odor are injected into the nasal passage or passages in sufficient volume and with sufficient force. The investigations demonstrated that, in order that the injection shall be effective, the pressure under which the air and odor reach the olfactory receptors is of more importance than the volume. The olfactory tests with the blast injection of odors are based on this new principle. In all previous methods for testing the olfactory sense the odor was inhaled. In the procedure of blast injection of odors the air and odor are injected into one or both nasal passages during a period of voluntary cessation of breathing—the force of the injection taking the place of the nasal inhalation.

Methods and Material.—The smallest volume of odor injected into one nasal passage during cessation of breathing that can be recognized before a breath is taken is called the minimum identifiable odor (M. I. O.) of the substance used. Each odorous substance has its own M. I. O., and, within certain limits, the M. I. O. of any odorous substance is the same for all healthy persons. The test of the sense of smell with the blast injection of odors during periods of voluntary apnea is therefore a quantitative procedure.

A large number of odorous substances were studied. Some were chemically pure; others were compounds. Finally, ground coffee and citral were selected for clinical use, for the following reasons: Both substances have a familiar odor, and both have a fairly constant M. I. O. The odor of coffee is due to several aromatic substances, but we found that a high grade commercial brand of coffee has a fairly constant olfactory value. If the brand of coffee is changed, the M. I. O. must be established by tests on a number of normal persons. Freshly roasted coffee or that kept in a closed tin contains aromatic substances freed by the roasting which may lower the M. I. O. Therefore a fresh supply of coffee must always be exposed to the air for a few hours before it is used for olfactory

tests. We have found it practical to blow air through the test bottle containing a fresh supply of ground coffee for ten or fifteen minutes before using the bottle for olfactory tests. Even if the bottle is used daily, the coffee need be replaced only every one or two months.

As far as its odor is concerned, citral is stable, and one supply can be used for several months without any change in its olfactory value. Citral is a valuable substance for olfactory tests because its odor—lemon or lime—is familiar and because it affects also the trigeminal nerve endings in the nasal passages and can therefore be used to test the sensibility of the trigeminal nerve.

The test bottles have rubber stoppers and connecting tubes, and rubber has a slight odor. As the odor of rubber has a higher M. I. O. than that for either coffee or citral, the rubber stopper and connections used on the test bottles do not interfere with tests in which the olfactory values of coffee and citral are determined. For clinical use, therefore, it is permissible to use pure rubber connections. In our tests the odor of rubber was almost never recognized or mentioned either by normal persons or by patients who were being tested.

TABLE 1.—*Results of Olfactory Tests on 150 Patients with Tumor of the Brain*

Location of Growth	Number of Patients	Patients with Tumors Correctly Localized by Olfactory Tests		Patients with Tumors Not Localized by Olfactory Tests	Patients with Tumors Incorrectly Localized
		Number	Percentage		
Frontal region	51	44	86.3	7	0
Pituitary gland	32	16	50	16	1
Temporal region	7	6	85.7	1	0
Parietal and occipital regions	14	8	57.1	5	1
Parasagittal region	9	5	56	3	1
Corpus callosum	4	2	50	1	1
Bucconeural pouch	2	0	0	2	0
One cerebral hemisphere (not frontal portion)	14	10	71.4	4	0
Subtentorial region	17	6	35	10	0

The method by which the tests are carried out and the apparatus that is required have been described in detail in papers already published.[1] In these papers there was described also a second procedure, called the stream injection of odors, which was found to be useful for the production of olfactory fatigue. These two procedures—the blast injection of odors as a quantitative test of olfactory acuity and the stream injection of odor followed by blast injection as a test of olfactory fatigability—were found to be of value for the localization of tumors of the brain.

LOCALIZATION OF TUMORS OF THE BRAIN BY OLFACTORY TESTS

A summary of the results of the olfactory tests on 150 patients with tumor of the brain is given in table 1.

1. Elsberg, C. A.: A New and Simple Method of Quantitative Olfactometry, Bull. Neurol. Inst. New York **4**:1, 1935; Olfactory Fatigue, ibid. **4**:479, 1935. Elsberg, C. A.; Levy, I., and Brewer, E. D.: The Trigeminal Effects of Odorous Substances, ibid. **4**:270, 1935; The Odorous Substances to Be Used for Tests of the Olfactory Sense, ibid. **4**:286, 1935. Elsberg, C. A., and Brewer, E. D.: A Detailed Description of the Technique of Two Olfactory Tests Used for the Localization of Supratentorial Tumors of the Brain, ibid. **4**:501, 1935.

For a full appreciation of the significance of these figures, attention must be directed to the following facts: 1. The olfactory tests have no value for the localization of tumors in the posterior cranial fossa, although they may be of use for the differentiation of frontal and cerebellar growths. Subtentorial growths are included in table 1 for the sake of completeness. 2. In the large majority of instances the localization of a pituitary tumor is made without difficulty from the glandular and neighborhood disturbances and from the roentgenologic evidence of characteristic enlargement of the sella turcica. Pituitary growths can be localized by olfactory tests only when they are of sufficient size to exert pressure on the extracerebral olfactory pathways. Olfactory tests were made on a large number of patients with pituitary tumor in order to learn whether the growth was still entirely within the sella turcica or whether it had extended above the level of the diaphragm of the sella. The results of olfactory tests on patients with pituitary adenoma showed that in about one half there was no evidence of pressure on the olfactory pathways. In these patients, therefore, the growth was small and was confined below the sellar diaphragm.

In order to arrive at a conclusion regarding the value of these new olfactory tests for the localization of supratentorial tumors of the brain, cases of subtentorial and pituitary growths (in which the tests are not used primarily for localization) must be excluded. When the figures in table 1 were analyzed from this point of view they yielded the following results:

Total no. of supratentorial tumors	101	
No. correctly localized by olfactory tests	75	(74.2%)
No. without evidence of localized lesion by olfactory tests	23	(22.9%)
No. incorrectly localized by olfactory tests	3	(2.9%)

In the case of tumors in or around the frontal lobes, the growth was accurately localized in over 86 per cent of the patients. By accurate localization is meant the conclusion as to whether the growth was underneath or within the substance of one or the other lobe and whether it was in or near the midline.

In the case of tumors in the parietal and occipital lobes, more especially the parasagittal meningiomas and gliomas and tumors of the corpus callosum, localization was possible in from 50 to 71 per cent of the patients. In these patients the results of the olfactory tests made it possible to conclude: (1) that the growth was in one or the other cerebral hemisphere, (2) that the frontal lobe was probably not involved and (3) that the growth was or was not deeply situated near or in the midline.

OLFACTORY PATTERNS ASSOCIATED WITH TUMORS IN VARIOUS SITUATIONS

By olfactory pattern is meant the group of values for the M. I. O. and the duration of fatigue on the two sides.

The olfactory patterns most often observed in patients with supratentorial tumors are given in table 2.

In patients with extracerebral growths underneath the frontal lobes the M. I. O. was usually elevated on one or both sides, but olfactory fatigue was not prolonged beyond the normal. In the case of unilateral growths of small size the M. I. O. was elevated only on the side of the lesion, but if the growth was large or extended across the midline there was bilateral elevation of the M. I. O., or even anosmia. If the elevation was bilateral it was usually greater on the side on which all or the greater part of the tumor was situated.

If the growth was very large and had buried itself in one or the other frontal lobe, the M. I. O. was elevated, and the fatigue was prolonged on the same side. Such growths may cause an olfactory pattern which is similar to that for a tumor within the substance of the brain.

The characteristic feature of the olfactory pattern associated with tumors of the frontal lobes was elevation of the M. I. O. This elevation may be due to direct or transmitted pressure on the olfactory nerves, bulbs or tracts or the external or internal olfactory roots. We suspect also the pressure on the anterior commissure may produce the same, and usually a bilateral, effect.

A tumor in or underneath one temporal lobe might extend forward to the frontal lobe and cause elevation of the M. I. O. on that side.

The olfactory pattern characteristic of growths that did not involve the frontal lobes was no elevation of the M. I. O. and was based on the comparative fatigability of the two sides. The more deeply situated the neoplasm the longer the duration of fatigue on the side involved. The more rapidly a tumor had grown and the greater the associated swelling of the affected lobe, the greater the probability that the olfactory tests would show prolongation of fatigue. Some patients with slowly growing tumors—especially the parasagittal meningiomas—of the parieto-occipital region showed fatigability within normal limits, and these were the patients in whom, more especially, the olfactory tests failed to localize the lesion.

OLFACTORY PATTERNS IN ABSENCE OF EVIDENCE OF A LOCALIZED LESION

In 23 patients (22.9 per cent) with tumors of the brain the olfactory tests failed to show any evidence of a localized lesion. In 14 of these, the M. I. O. was not elevated, and the duration of fatigue was within

TABLE 2.—*Olfactory Patterns in Patients with Supratentorial Tumor*

Situation of Tumor	M. I. O.		Duration of Fatigue*	
	Side of Tumor	Opposite Side	Side of Tumor	Opposite Side
1. Subfrontal region	Elevated for coffee and citral	Not elevated	Normal	Normal
	Elevated for coffee and citral	Elevated for coffee and citral	Normal	Normal
	Elevated for coffee or citral	Not elevated	Normal	Normal
	Elevated for coffee or citral	Elevated for coffee or citral	Normal	Normal
	(More rarely, if large)			
	Elevated for coffee and citral	Elevated for coffee and citral	Prolonged for coffee and citral	Normal
2. Frontal region	Elevated for coffee and citral	Not elevated	Prolonged for coffee and citral	Normal
	Elevated for coffee and citral	Elevated for coffee and citral	Prolonged for coffee and citral	Normal
	Elevated for coffee or citral	Not elevated	Prolonged for coffee and citral	Normal
	(More rarely)			
	Elevated for coffee or citral	Elevated for coffee or citral	Prolonged for coffee or citral	Prolonged for coffee or citral
	Elevated for coffee or citral	Not elevated	Prolonged for coffee and citral	Prolonged for coffee and citral
	Elevated for coffee or citral	Elevated for coffee or citral	Not prolonged	Not prolonged
3. Temporal region	Not elevated	Not elevated	Prolonged for coffee and citral	Not prolonged
	Not elevated	Not elevated	Prolonged for coffee or citral	Not prolonged
	Not elevated	Not elevated	Prolonged for coffee and citral	Less prolonged for coffee or citral
4. Frontotemporal region: Various combinations of 1, 2 and 3				
5. Parietal and occipital regions	Not elevated	Not elevated	Prolonged for coffee and citral	Normal
	Not elevated	Not elevated	Prolonged for coffee or citral	Normal
6. Para-sagittal region and corpus callosum	Not elevated	Not elevated	Much prolonged for coffee and citral	Normal
	Not elevated	Not elevated	Much prolonged for coffee and citral	Less prolonged for coffee and citral
	Not elevated	Not elevated	Much prolonged for coffee and citral	Much prolonged for coffee or citral
	Not elevated	Not elevated	Much prolonged for coffee or citral	Much prolonged for coffee or citral
	Elevated for coffee and citral	Not elevated	Much prolonged for coffee and citral	Much prolonged for coffee and citral
	Elevated for coffee and citral	Not elevated	Much prolonged for coffee or citral	Less prolonged for coffee or citral
7. Cerebral hemisphere	Not elevated	Not elevated	Prolonged for coffee and citral	Normal
	Not elevated	Not elevated	Prolonged for coffee or citral	Normal

* "Much prolonged" means fatigue for ten minutes or more.

normal limits. In the remaining 9 patients, fatigue was prolonged on both sides for either coffee or citral, or fatigue was prolonged on one side for one substance and on the opposite side for the other substance.

OLFACTORY PATTERNS IN 4 PATIENTS WITH TUMORS INCORRECTLY LOCALIZED BY THE OLFACTORY TESTS

The findings in the following cases are described in detail:

CASE 1.—R. L., a man with a large cystic pituitary adenoma, had received much roentgen therapy. He had typical primary atrophy of the optic nerve, with bitemporal defects in the visual fields and a much enlarged sella turcica. Except for the glandular and neighborhood signs, there were no objective neurologic disturbances.

Olfactory Tests.—The M. I. O. was normal, but fatigue for both coffee and citral was much prolonged on both sides. This was the pattern that is frequent with a lesion in the midline or in both cerebral hemispheres. We have no explanation for the results of the olfactory tests.

CASE 2.—I. H., with an astrocytoma of the left temporal and occipital lobes, was admitted with a history of headache of one month's duration, disturbances in speech and difficulty in mental concentration. The main objective disturbances consisted of motor and sensory aphasia, right homonymous hemianopia, low grade papilledema and slightly hyperactive tendon reflexes on the right side of the body.

Roentgenograms after the injection of air showed that the third and lateral ventricles were displaced to the right and depressed; a diagnosis of parasagittal tumor in the left parieto-occipital region was made by the roentgenologist.

Olfactory Tests.—The results are summarized in the following tabulation:

	M. I. O. for Coffee	M. I. O. for Citral	Fatigue for Coffee, Min.	Fatigue for Citral, Min.
Right side	7	8	Normal	Normal (?)
Left side	13	13	10+	7.5

The olfactory tests were interpreted as indicating a tumor deeply situated in the left frontal lobe.

The determination by olfactory tests of the hemisphere in which the growth was situated was correct, but the elevation of the M. I. O. on the left side indicated a frontal lesion. At operation a deeply situated tumor was partly removed from the left temporal and occipital lobes.

CASE 3.—J. W., aged 41, gave a history of symptoms for ten weeks following trauma to the head. There were left hemiplegia, with hyperactive tendon reflexes on the left side and a Babinski sign bilaterally; weakness of the right facial nerve of central type; low grade papilledema, and mental confusion. A subdural hematoma was suspected. The report after encephalographic examination was: "A parasagittal mass which encroached sharply on the left lateral ventricle and the roof of the third ventricle." Roentgenographic diagnosis was right subdural hematoma or parasagittal tumor in the right posterior frontal region.

The olfactory tests showed a normal M. I. O. for both coffee and citral and much prolonged fatigue for coffee and citral on the left side. The olfactory findings were interpreted as indicating a lesion near or in the midline on the left side.

Trephine openings were made on the right side, and a bone flap was then turned down as an emergency operation; there was no evidence of a subdural hematoma or neoplasm. The patient's condition was so poor that an exploration could not be made on the left side. The patient soon succumbed, but permission for an autopsy could not be obtained.

The signs and symptoms and the pneumograms pointed to a lesion in the right hemisphere, near the midline, while the olfactory tests indicated a lesion on the left side. Although no evidence of a lesion on the right side was observed at operation, and therefore a left subdural hematoma was still a possibility, we have included this case as one in which there was incorrect localization by the olfactory tests.

Case 4.—A young man had signs which pointed to a parasagittal meningioma on the right side. He had a small hyperostosis of the skull, to the right of the midline, in the posterior frontal region. The roentgenographic diagnosis was parasagittal meningioma in the right precentral region.

Olfactory Tests.—The results are summarized as follows:

	M. I. O. for Coffee	M. I. O. for Citral	Fatigue for Coffee, Min.	Fatigue for Citral, Min.
Right side	12	10	Normal	Normal
Left side	12	13	Normal	Prolonged on one examination, normal on second examination

The olfactory tests indicated a frontal tumor underneath the frontal lobes. At the operation a parasagittal meningioma, adherent to the longitudinal sinus and falx, was removed from the right precentral area.

OLFACTORY FINDINGS IN 150 PATIENTS WITH CEREBRAL SYMPTOMS NOT DUE TO TUMOR

A summary of the results of the olfactory tests in this group is given in table 3.

In order to evaluate the results of the olfactory tests shown in table 3, one must remember that these are functional tests which may indicate a localized lesion other than a tumor. Thus, in 6 patients with encephalitis, 1 with serous meningitis, 3 with cerebrospinal syphilis and 7 with a variety of other lesions both the olfactory tests and the neurologic examination indicated that there was a localized lesion.

MOST FREQUENT OLFACTORY PATTERNS IN INTRACRANIAL DISEASE OTHER THAN TUMOR

When the tests indicated that there was a localized lesion the olfactory patterns were similar to those in patients with tumor of the brain.

When the tests gave no evidence of a localized lesion the most frequent olfactory patterns were as follows:

M. I. O.	Fatigue
Not elevated	Not prolonged
Not elevated	Prolonged on both sides for coffee and citral or for only one of the substances
Not elevated	Slightly prolonged on one side for coffee or for citral
Elevated on both sides for coffee and citral	Prolonged on one or both sides for one or both substances
Elevated on one side for coffee or citral	Prolonged on both sides for one or both substances and frequently for coffee on one side and for citral on the other side
Elevated on one side for coffee or citral.	Prolonged on the opposite side for citral or coffee

TABLE 3.—*Results of Olfactory Tests in 150 Patients with Cerebral Symptoms Not Due to Tumor*

Nature of Lesion	Number of Patients	Patients with Evidence of Localized Lesion	Patients with No Evidence of Localized Lesion	
			Number	Percentage
Convulsive seizures	54	10	44	82
Encephalitis	16	6	10	68
Vascular lesions	5	2	3	60
Multiple sclerosis	12	1	11	92
Headaches	12	0	12	100
Serous meningitis	6	1	5	83
Cerebrospinal syphilis	11	3	8	73
Paralysis agitans	3	0	3	100
Varia	31	5	26	84
Number of patients in whom there was evidence of a localized lesion				28 (18.7%)
Number of patients in whom there was no evidence of a localized lesion				122 (81.3%)

In the majority of patients who did not have an intracranial neoplasm nothing characteristic in the olfactory patterns was found. However, in some diseases certain patterns were frequent: 1. In paralysis agitans there was profound fatigability of the olfactory sense. In patients with this disease the M. I. O. for both coffee and citral was elevated on both sides, and fatigue was prolonged on both sides for both substances. 2. This marked fatigability was also found in some patients with encephalitis and cerebrospinal syphilis. 3. In 5 of 6 patients with serous meningitis the olfactory pattern was normal. 4. Patients with long-standing headache, in whom all examinations gave normal results, usually had marked olfactory hyperacuity. 5. In 3 patients with turricephaly there was bilateral elevation of the M. I. O., with normal fatigability.

DIFFERENTIAL DIAGNOSIS OF TUMOR AND OTHER DISEASES OF THE BRAIN BY OLFACTORY TESTS

In diffuse diseases of the brain the olfactory pathways may be affected both inside and outside the brain. Therefore, elevation of the M. I. O. may occur as the result of a lesion in the extracerebral pathways, as well as compression of these structures by a tumor. The olfactory pattern characteristic of tumor, however, is unusual in association with diffuse lesions of the brain, and the evidence of a localized lesion from olfactory tests is much more infrequent.

In 103 of 251 patients (101 with tumor and 150 with other diseases of the brain) the olfactory tests indicated a localized lesion. Seventy-five of these patients had a tumor. Therefore the olfactory evidence of a localized lesion gave a 73 per cent probability that the patient had a neoplasm.

The olfactory tests have some value for diagnosis in patients who have convulsive seizures without any evidence in roentgenograms or the fundi of an increase in intracranial pressure. Thus, of the patients in our series who had a tumor 21 had suffered from convulsive seizures for from a few weeks to three years without any clinical evidence of increase in intracranial pressure. Therefore, 21 patients were selected from the group with "epilepsy" who likewise had had convulsive seizures for less than three years. In 6 of the tumor group convulsions had occurred for less than one year; in 6, for from one to two years, and in 6, for from two to three years. Of the nontumor group, 8 had had convulsions for less than one year; 7, from one to two years, and 6, from two to three years. The two groups were therefore comparable.

In 18 of the 21 patients in the tumor group the olfactory tests indicated a localized lesion, while of the 21 patients in the nontumor group a localized lesion was indicated in 6. Of the entire group of 42 patients a localized lesion was indicated in 24, but in 18 of this number the lesion was a tumor. It was concluded from this small series that in a patient with convulsive seizures for less than three years and no clinical evidence of increase in intracranial pressure the olfactory evidence of a localized lesion gave a 75 per cent probability of a neoplasm.

In a paper published recently [2] attention was called to the fact that the olfactory tests may be of aid in the differentiation of aneurysm of the internal carotid artery and pituitary tumor.

Therefore, there is evidence that olfactory tests have some value for differential diagnosis.

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2. Elsberg, C. A., and Stewart, J.: A Note on the Value of Tests of Olfactory Acuity for the Diagnosis of Pituitary Tumor, Bull. Neurol. Inst. New York **6**:126, 1937.

SUMMARY

An analysis was made of the results of olfactory tests in 300 patients—150 with tumor and 150 with some other disease of the brain.

The olfactory tests have no value for the localization of subtentorial tumors.

Of 101 patients with supratentorial tumors, the growth was localized by the olfactory tests in 74 per cent, not localized in 22.9 per cent and incorrectly localized in 2.9 per cent.

Growths underneath or in the frontal lobes were localized in 86 per cent of the patients.

In 81 per cent of 150 patients who did not have a tumor the olfactory tests gave no evidence of a localized lesion.

If the olfactory tests indicated that there was a localized lesion there was a 73 per cent probability that the patient had a neoplasm.

In a series of 42 patients with convulsive seizures for less than three years without any clinical evidence of increased intracranial pressure the finding of a localized lesion by olfactory tests gave a 75 per cent probability that the patient had a neoplasm.

The olfactory patterns most frequently found in patients with and without tumor have been described.

The quantitative olfactory tests with the blast injection and stream injection of odors have value not only for the localization but also for the diagnosis of supratentorial tumors of the brain.

MARGINS OF THE OPTICALLY EXCITABLE CORTEX IN THE RABBIT

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Kornmüller,[1] in recording the spontaneous electrical activity of the cerebral cortex in several mammals (rabbit, cat and ape), interpreted his findings as indicating that fields of the cerebral cortex known to differ in their cytoarchitectonic pattern differ likewise in the wave pattern obtained. The present report is concerned with the architectonic limits of the optically excitable cortex of the rabbit, i. e., the area of cortex in which a characteristic pattern of activity interrupts the spontaneous fluctuations following application of single stimuli to the contralateral optic nerve.

With the animal under light ether anesthesia, the optic nerve, after removal of the eye, was stimulated directly by single maximal electrical shocks, each stimulus resulting in a single volley of impulses in parallel fibers passing over the pathway as nearly synchronously as possible. The pathway consists of the optic nerve and tract (most of which crosses in the rabbit chiasm), the dorsal nucleus of the lateral geniculate body, the optic radiation and a sequence of cellular elements situated in the layers of the cortex. The preparation and manipulation of the animals have been described in previous publications (Bartley and Bishop[2]).

TECHNIC

Fifteen rabbits were used in the study; diagrams for 10 of them are presented. In series A, of 5 animals (fig. 1, *1* to *5*), the response was recorded between an indifferent electrode placed on the adjoining bone and a local electrode placed on the surface of the cortex. The latter was a no. 10 sewing needle bent at a right angle; its blunt point, supported by a ring of insulating cement, was moved progressively from the center of the area striata (Rose[3]) across the fissura

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1. Kornmüller, A. E.: Die bioelektrischen Erscheinungen architektonischer Felder der Groszhirnrinde, Biol. Rev. **10**:383-426, 1935.

2. Bartley, S. H., and Bishop, G. H.: The Cortical Response to Stimulation of the Optic Nerve in the Rabbit, Am. J. Physiol. **103**:159-172, 1933.

3. Rose, M.: Cytoarchitektonischer Atlas der Groszhirnrinde des Kaninchens, J. f. Psychol. u. Neurol. **43**:353-440, 1931.

sagittalis lateralis (Winkler and Potter [4] and fig. 2, *6*) toward the midline. In series B, of 5 animals, the indifferent electrode consisted of a needle, insulated except at the tip, thrust beneath the center of the optically excitable area, almost to the ventricle. In 2 animals (figs. 2, *7* and *8*, and 4) the amplitudes of three characteristic potential waves in the response were measured (Bartley and Bishop [2]). The local electrode was placed consecutively at points progressing from the approximate anatomic center of the area striata anteriorly across the margin on a parasagittal plane and medially across the margin on a frontal plane. In another animal of series B (fig. 3, *11*) the activity at points on the frontal and parasagittal planes was similarly measured, and random points were taken on the lateral margin. However, in this animal only the height of the third wave in the response was recorded. In the remaining 2 animals (fig. 3, *9* and *10*) the waves from the lateral, medial and anterior margins and from one point on each of the posterior margins were recorded. In series C, of 5 animals, variants of these procedures were carried out, the information obtained being in all essentials confirmatory of that presented for the first two series. The results for series C were not plotted.

In all animals, measurements and identifying stabs for allocating later the recorded points in serial sections were obtained and the blocks prepared for histologic study as a control. They were fixed for twenty-four hours in a mixture of saturated mercury bichloride and absolute alcohol, washed, dehydrated, cleared in xylene, embedded in paraffin and sectioned serially in a frontal plane, at 10 or 20 microns. For the animals of series A and C, only the zone of the optically excitable cortex which passed through the frontal plane measured was examined. For series B, the serial sections passed entirely through the optically excitable cortex and likewise made available a generous margin of the adjoining fields medial, anterior and lateral thereto.

CYTOARCHITECTONIC MARGINS

The readily available cytoarchitectonic atlas of the rabbit brain compiled by Rose [3] furnishes a convenient guide to the observations made in the present study. On a series of photographs (magnified 20 diameters) of frontal sections of the rabbit brain at 20 microns (selected from 20 to 50 sections apart) Rose has indicated the boundaries of the cytoarchitectonic fields; references to sketches of the surfaces of the brain illustrate the approximate extent of each field. It is with the cytoarchitectonic area designated by Rose as the area striata (area 17, Brodmann [5]) and its contingent fields that we are particularly concerned, since the evidence afforded by Putnam and Putnam [6] and others indicated that this striate field receives the projection of the dorsal nucleus of the lateral geniculate body (optic radiation).

4. Winkler, C., and Potter, A.: An Anatomical Guide to Experimental Researches on the Rabbit's Brain, Amsterdam, W. Versluys, 1911.

5. Brodmann, K.: Vergleichende Lokalisationslehre der Grosshirnrinde, Leipzig, J. A. Barth, 1909.

6. Putnam, T. J., and Putnam, I. K.: Studies of the Central Visual System: I. The Anatomic Projection of the Retinal Quadrants on the Striate Cortex of the Rabbit, Arch. Neurol. & Psychiat. **16**:1-20 (July) 1926.

Reference to figure 2, *6*, a sketch of the dorsal surface of the rabbit brain slightly modified from Rose (fig. 3 of his text) illustrates the approximate extent of the area striata (*Str*), which appears in Rose's plates 11 to 19. It is bounded medially by the area peristriata (*Pstr*), which lies beneath the fissura sagittalis lateralis and separates the area striata from the dorsomedially placed field called the area retrosplenialis granularis dorsalis (*Rsg β*). The anterior boundary is the area parietalis 3 (*Par 3*), and the lateral border, the area occipitalis (*Oc*); the field extends to the posterior pole of the cerebral hemisphere.

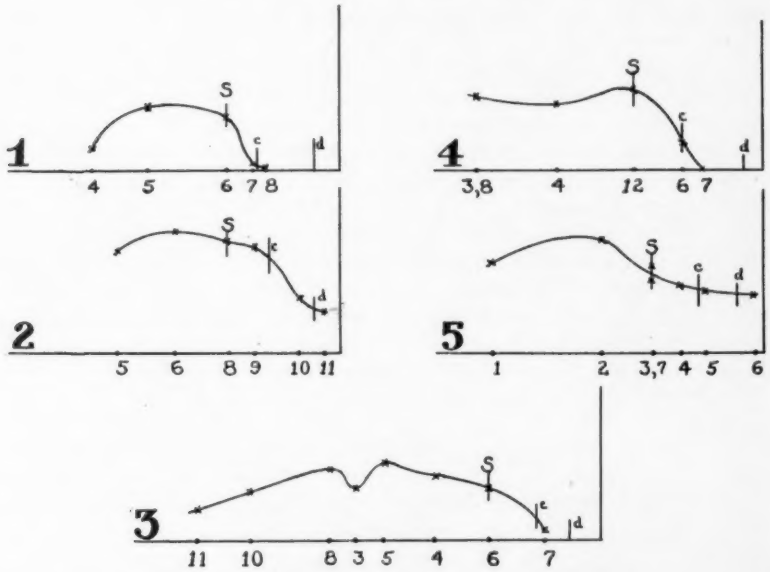


Fig. 1 (series A).—In the 5 experiments recorded, the margin between the retrosplenial and the striate territory was plotted physiologically as the line where the amplitude of cortical potential records resulting from stimulation of the contralateral optic nerve fell to zero. The tissue used in each experiment was later sectioned and stained by the Giemsa method. In the graphs, dots on the base line represent the spacing of points along a straight line across the margin in question from which the records were obtained. Above each dot is plotted the amplitude of the main wave of the potential record for that point, each value being the average of at least three responses. Numerals below the base line indicate the order in which the records were taken; missing numerals correspond to records from points not located on the line across the cortical margin which was plotted. *S* indicates the location of the fissura sagittalis lateralis in a section just anterior to the middle of the optically excitable cortex; *c*, a point in this section marking the most lateral extent of the fine granules characteristic of the retrosplenial territory, and *d*, a point at which stratification of the cortex attained completely the characteristics of the retrosplenial territory. The space from *c* to *d*, therefore, represents a cytoarchitectonic transition zone. These 5 experiments were performed serially and represent a random selection. The distance from the fissure to the midline was approximately 4 mm. in each preparation.

Rose has given in terms of Brodmann's [5] six layer plan the relative characteristics which serve to distinguish the area striata from the adjoining fields. I, the lamina zonalis, is thin. II and III, the lamina granularis externa and lamina pyramidalis, together make up a layer of medium width having a dense population of relatively small cells. IV, the lamina granularis interna, is wide and contains densely packed round, angular and pyramidal cells. It is divisible into an outer, less densely populated layer, IV a, and an inner, more densely populated layer, IV b. V, the lamina ganglionaris, is relatively thin and is divisible into an outer, densely populated layer, V a, and an inner, less populated layer, V b. In both, medium-sized to large pyramidal cells occur, the larger predominating in V a and the smaller in V b. VI, the lamina multiformis, is relatively wide and contains relatively large cells, closely packed. It is divisible into an outer, less densely populated layer, VI a, and an inner, more densely populated layer, VI b.

Rose characterized the lateral transition from the area striata to the area occipitalis as sharp posteriorly and less sharp anteriorly. The principal differences are as follows: In layers II and III of the area occipitalis the cells are of medium size and less densely packed than in the area striata. Layer IV is thinner and less densely populated and has relatively fewer granules. V is wider, but shows the same division into an outer, more densely populated layer, V a, having larger cells, and an inner, less densely populated layer, V b, having smaller cells. Layers VI a and b are thinner than in the area striata and have a population of smaller cells, somewhat less densely packed.

Rose defined the area peristriata as a transition from the area retrosplenialis granularis dorsalis to the area striata. Layer I is relatively wide as compared with the corresponding layer in the area striata. Layers II and III are thinner and less densely populated, with small and medium-sized cells. IV is thinner and less densely populated than the similar layer in the area striata and contains small round cells in addition to the granules. V is of medium width and is divisible into an outer, more densely populated layer V a, and an inner, less densely populated layer, V b. Both contain medium large and large pyramidal cells. VI is thinner than the corresponding layer in the area striata.

Because the area retrosplenialis granularis dorsalis is important in considering the medial topographic limit of the optically excitable cortex, a brief résumé of its appearance is likewise taken from Rose. Layers II, III and IV are grouped together and divided into an outer, large cell sublayer, a, and an inner, granule-containing sublayer, b. V is very wide and contains radially oriented medium-sized large pyramidal cells. VI is divisible into sublayers a and b.

Anteriorly, the area striata is limited by the area parietalis 3. The difficulty in drawing a sharp line between the two fields is indicated by the transition zone of Rose's plate 10, section 738. In the area parietalis 3 lamina I is wider than in the area striata and II and III are thinner and more sparsely populated, with small pyramidal cells. IV is thin and sparsely populated, with granules. V is the widest layer. Thin, relatively clear zones (V a and V c) separate the remainder of layer V b from layer IV above and layer VI below. In layer V b the cells are the large pyramidal type; in layers V a and V c they are less closely spaced. Layer VI has two sublayers, of which VI b contains the larger cells.

We plotted the margins of the optic cortex by two sets of criteria, histologic and physiologic. First, making use of the parcellation of Rose, we entered the significant cytoarchitectonic boundaries at a mag-

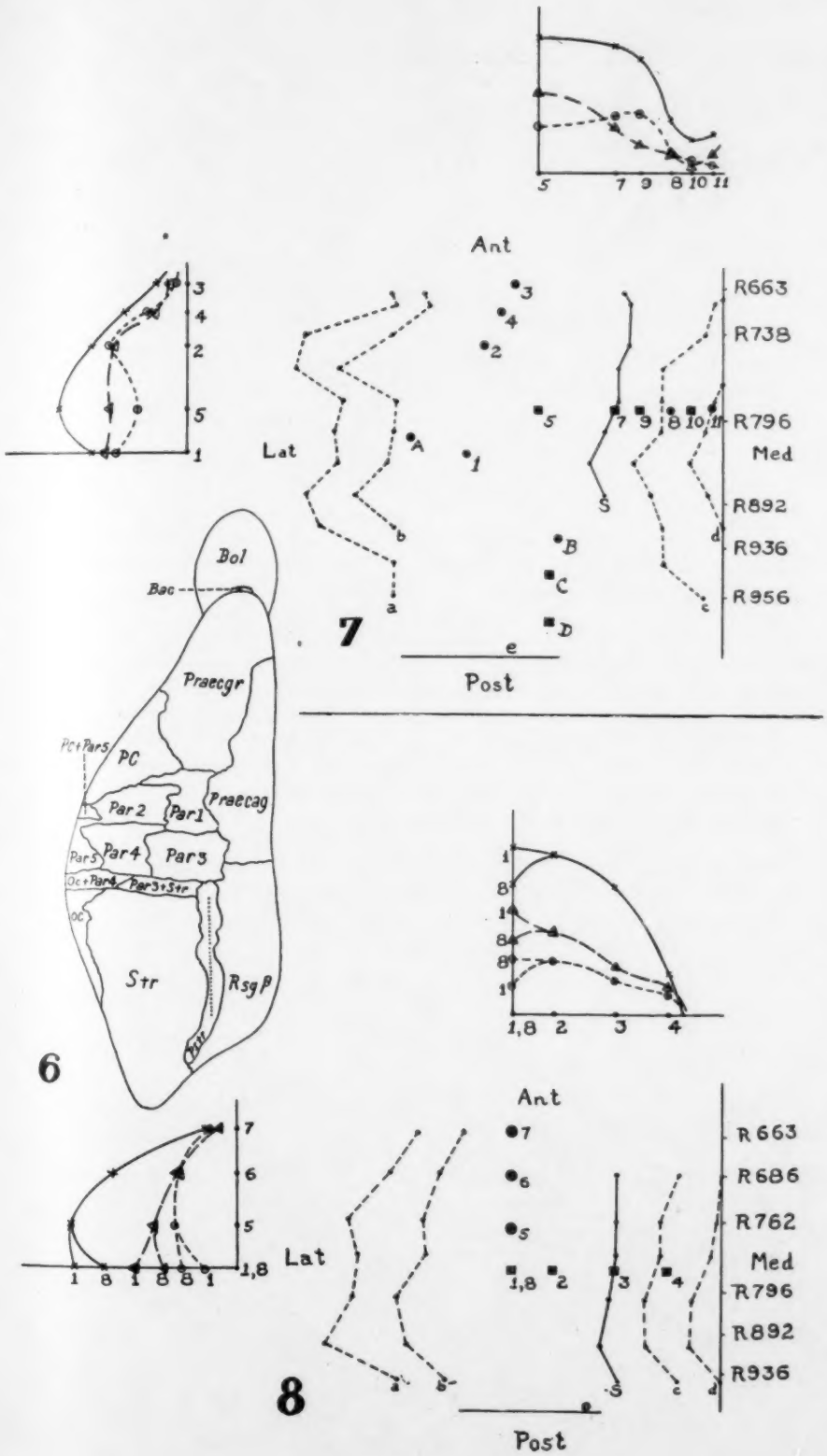
EXPLANATION OF FIGURE 2

In *6* appears a sketch of the dorsal surface of the cerebral hemisphere of the rabbit, taken from Rose's atlas to illustrate his cytoarchitectonic parcellation. The original sketch was modified by adapting its mirror image to the left cerebral hemisphere, on which the present study was carried out. We have designated by a dotted line following the long axis of the peristriate field (*Pstr*) the position of the fissura sagittalis lateralis, as determined from Rose's photographs of frontal sections of the rabbit brain.

7 and *8* (series B) are diagrams showing the limits of the optically excitable area. Each figure includes three parts. Centrally placed is an anatomic plot of the cortex from serial sections. Above this is a graph of the amplitudes of the physiologic record along the row of points extending transversely across the medial cortical margin. To the left is a graph of the amplitudes from a second row of points perpendicular to the first.

On the central map, closed circles indicate points which were marked immediately after recording with shallow stab wounds, which did not penetrate to the basal white matter. Closed squares show points similarly recorded which were located by measurements from stab wounds on frontal sections. Numerals indicate the order in which the records were taken. On the line to the right, indicating the median plane, the approximately equivalent section numbers from the Rose atlas have been entered. The unbroken line, *S*, locates the fissure and measures the distance from the fissure to the midline. Lines *a* and *b* measure, respectively, the distances from the midline to the outer and the inner margin of the transition zone between the occipital (*Oc*) and the striate (*Str*) field, obtained from histologic sections. Lines *c* and *d* indicate, respectively, the outer and the inner margin of the transition zone between the peristriate (*Pstr*) and the retrosplenial (*Rsg* β) field, in the section. *e*, the last section of the block, passed through the posterior pole of the cortex in *7* and somewhat anterior to the pole in *8*.

Above each chart of the area in *7* and *8* are plotted the amplitudes of the record corresponding to the points in a line perpendicular to the medial plane. To the left of each record are plotted the amplitudes of points in a line parallel to this plane, the amplitudes being plotted at right angles to those in the first graphs. On each of the inset figures, the line *x* indicates the first (positive) response; the line with open circles and enclosed dots, the second (negative) wave, and the line with open triangles and enclosed dots, the third (positive) wave (fig. 4). Values for point *5* in *7* and for *1,8* in *8*, at the angle of the two lines, appear in both graphs. Points *A* to *D* were not on the lines plotted. *B* gave a response of high amplitude; *A* and *C*, a slightly lower response, and *D*, hardly any response, indicating an abrupt physiologic margin just posterior to *D* and somewhat lateral to *A*.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Par4
Par3
Str
Rsg β
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R762
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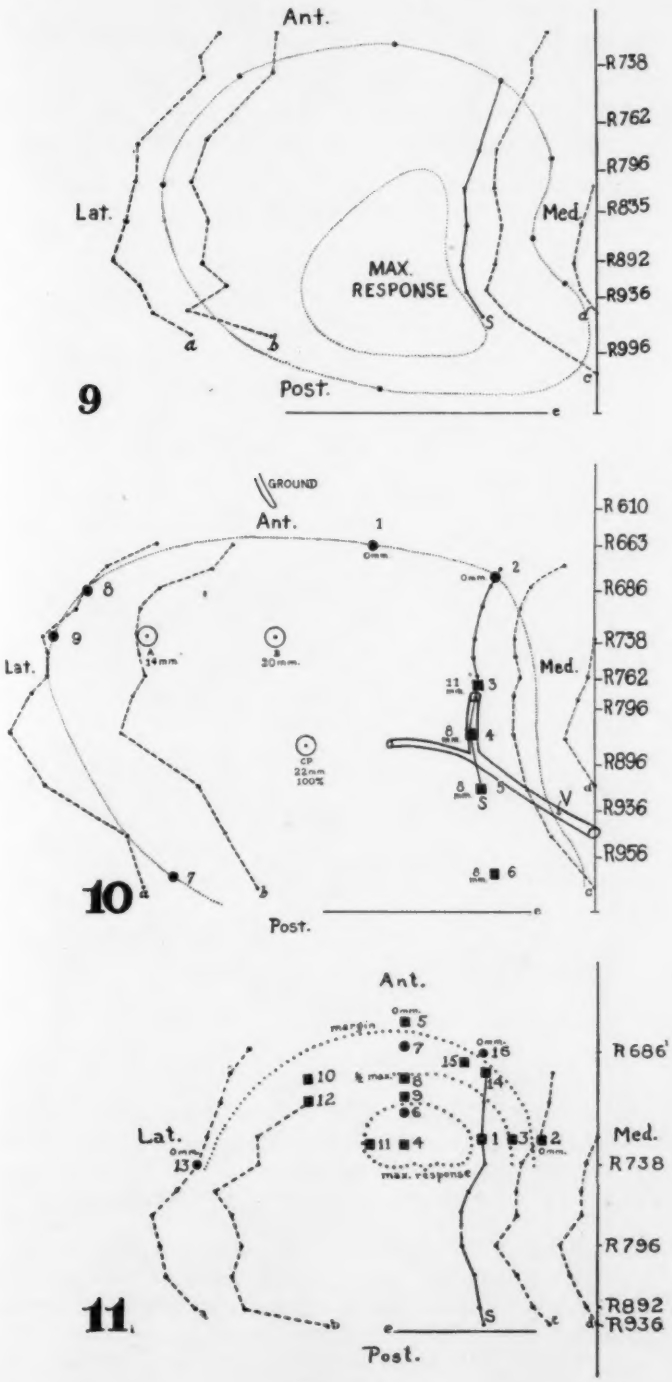
R892
R936
8

Figure 2.

EXPLANATION OF FIGURE 3

Sketches *9*, *10* and *11* (series B) represent 3 experiments in which the margin of the optically excitable area was mapped physiologically and the margin of the striate area was mapped histologically. On the charts, by measurements from the sections, the lateral transition zone, *a* to *b*, the medial zone, *c* to *d*, and the sulcus, *s*, were drawn, distance being taken from the midline. The midline is represented by the full line at the right margin of the figure, and along it the numbers indicate approximately corresponding sections in Rose's atlas. The points at which the response at the margin of the excitable area was zero are marked by dots of exaggerated size and are connected by a dotted line. Other designations are similar to those in *7* and *8* (fig. *2*). In *9* and *11* the areas of maximal response are likewise encircled by dotted lines. In *9* the posteromedial bulge is indicated as it appeared in numerous experiments, many of which have not been reported. In *10* the entire medial margin is similarly entered. In *9* and *10* the last section, *e*, passed through the posterior pole of the cortex, and in *11*, somewhat anterior to it. Note that the margins of the optically excitable area fall usually within the histologic transition zone medially and laterally but leave this zone anteriorly, cutting through an area which is little different architectonically from the striate area (see text).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GROUND
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Lat.
Med.
Post.
R 610
R663
R686
R738
R762
R796
R896
R936
R956
10
Ant.
Lat.
Med.
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R686
R738
R796
R892
R936
11

Figure 3.

nification of 10 diameters on cross section paper, allowing 1 mm. in the anteroposterior plane for each 5 sections of 20 microns each. Second, we plotted on these charts the physiologic data obtained from records made at points near these margins. The significance of a comparison of the two sets of data depends on further consideration of their details.

In the graphs for series B, the position of the fissura sagittalis lateralis and the lateral extent of the area striata were entered. Since it was not easy to

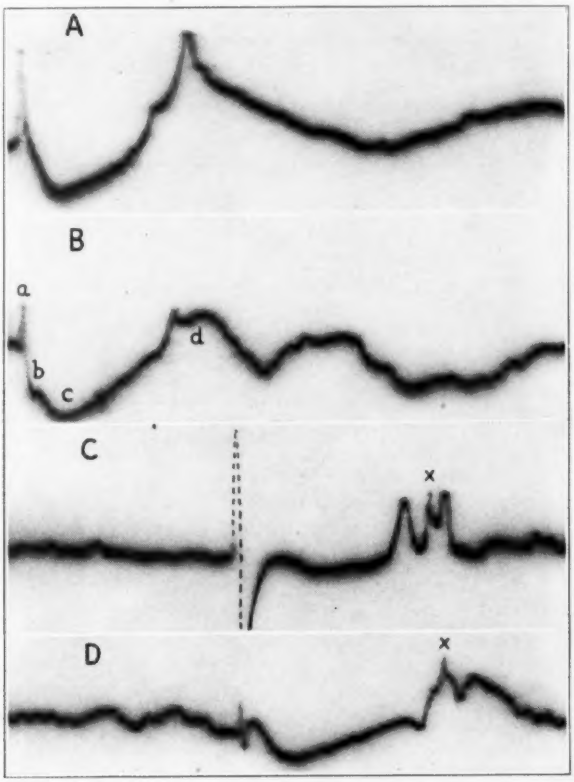

Fig. 4.—Typical action current responses of the optically active cortex of the rabbit to single stimuli applied to the contralateral optic nerve. *A* shows a relatively simple response; *B*, one in which there is repetition of the last wave; *a* a surface-positive phase of the diphasic process, and *b*, a negative phase not apparent in *A*. These two waves are superposed on the first wave of the triphasic process. *c* is the second, or negative, wave of the triphasic process, and *d*, the third, or surface-positive, wave of the same process. *C* and *D* are records from leads across the upper and the lower half of the cortex of another rabbit. In *C* one electrode was on the surface, and the other, at the margin between the lamina pyramidalis and the lamina granularis interna. In *D* the upper electrode was in the lamina granularis interna, and the lower electrode, in the basal white matter. *x* is a shocklike time signal superposed on the record of activity, one-fifth second after the stimulus.

determine within from 1 to 2 mm. the exact limit between the area striata and the area occipitalis, two points for the lateral boundary were entered, the one (*b*) indicating the beginning and the other (*a*) the terminus of the transition zone between the two fields. Likewise entered medially were two sets of points, one locating the most lateral extent of the granules of the area retrosplenialis granularis dorsalis (*c*), sublayer b of layers II, III and IV of the Rose designations, and the other indicating the point at which, in our opinion, the granules became sufficiently dense to constitute a definite layer (*d*). The cortices of the 5 animals in series A, on which the medial margin alone was measured by electrophysiologic methods, were plotted from the sulcus to the midline, since knowledge of the lateral margins was not significant in these cases. The boundary which concerns one here is that between the area peristriata and the area retrosplenialis granularis dorsalis, since in all cases in which the lateral margin of the retrosplenial territory was plotted the medial limit of the optically excitable cortex fell approximately at this line. That is, we could find in the rabbit no functional criteria which would give significance to a cytoarchitectonic differentiation between the striate and the peristriate cortex.

The stab wounds, used to allocate points from which records were obtained, were entered on the histologic maps already described. These were entered as closed circles. Other recorded points, located by measurements from these stab wounds, were indicated as closed squares. When a sufficient number of points of minimal response were located at the periphery of the optically excitable cortex, it was possible to indicate the margin of the optic area by a dotted line.

Figures 5 (*13*, *14* and *15*) shows low power photographs of frontal sections of 20 microns, selected to illustrate the appearance of areas of the cortex considered significant in interpretation of the physiologic records. As in the plots of the area of the optically excitable cortex, the closed circle designates a point located by a stab wound, and the closed squares indicate points localized by measurements from the stabs. Point *1* (fig. 5, *15*) was actually located in a section somewhat caudal to the section photographed, but no significant difference in appearance between the locus so marked and the area about the actual stab wound was noted. In the figures, the arrows between the fissure (*S*) and the midline indicate the point where granules characteristic of the retrosplenial cortex were first detected (*c*) and the point where these granules, in our opinion, first formed a definite layer (*d*).

Figure 5, *13* is taken from a section which passed through point *5* of figure 3, *10*. It corresponds approximately in level to Rose's plate 15, section 936. Point *5* lies on the fissure, and a record 8 mm. in height was obtained, as compared with a record 22 mm. in height from the point of maximal response for this cortex. It is to be noted by comparison with figure 3, *10* that the cortex failed to respond to stimulation of the optic nerve just medial to the arrow *c*.

Figure 5, *14* is from a section through the row of points on the cortex of figure 2, *8*, which pass from the center of the optic area toward the midline. In level the section approximates that shown in plate 12,

section 796 of Rose. The decline in height between points *1,8* and *4* of the first (positive) response and the second (negative) and third (positive) waves is to be observed in the upper inset of figure 2, *8*. The decline for each component of the activated potential is gradual between point *1,8* and point *3* and is abrupt between point *3* and point *4*. On the contrary, the cortex diminishes abruptly in thickness between point *1* + 2 and point *3* and remains of constant thickness between point *3* and point *4*. Therefore, it does not seem that the diminution in height of the response between the central area of the optically active cortex and the midline is a function of cortical thickness.

Figure 5, *15* is from a section passing somewhat frontal to the anatomic center of the optically excitable cortex plotted in figure 2, *7*. It again corresponds approximately to the level of plate 12, section 796 of Rose. In this case, between point *5*, in the central area, and point *6* + *7*, at the fissure, there was practically no diminution in the first (positive) response and the second (negative) wave (upper inset, fig. 2, *7*). The third (positive) wave commenced to fall off with the beginning of the rapid thinning of the cortex approaching the sulcus. The extent of the cortical layers is indicated by the Roman numerals adjacent to point *5*.

PHYSIOLOGIC RECORDS

Since the precision with which the functional margin of the optically active cortex can be located by the method employed depends on the degree to which an electrode records only the activity immediately under it, the mechanics of recording enters into the result. The records for a given position of the localizing electrode were identical whether the indifferent lead was under the hippocampus or on the bone at the side of the aperture in the skull, and whether it was near one edge or the other of the optically active area. If a cut was made in a frontal plane across the excitable cortex, a lead from a position posterior to the cut gave no significant record unless within 1 mm. of active tissue.

The optically active area, showing histologically a transition zone along the margins, would be expected to show, as it did, a gradient in the amplitude of the record taken across these margins. The flatter the actual gradient of activity the less the record taken across it should be in error. The gradient was less steep than that from an artificially produced margin made by cutting through the central area of the optically excitable cortex. In general, the effect of a source of potential near an electrode in a mass of tissue should decrease as a function involving inversely the square of the distance. The effect of all the factors involved would be to flatten the marginal gradient of the record as compared with the actual gradient of activity—that is, to reduce the amplitude toward the center of the optically excitable cortex and to extend the effect of the potential somewhat beyond the actual margin.

The error so introduced was apparently less than 1 mm. There was a corresponding error in estimating the histologic margins of the transition zone. This histologic transition zone, however, was at least 2 mm. wide, and the observation that the physiologic margin usually fell within this zone is presumably reliable.

The shape of the optically excitable area should be unaffected by these considerations, since the error in defining it should be uniform around the periphery. The outline obtained by functional means differed more significantly in shape than in proportion from that determined by Rose (fig. *2, 6*), using cytoarchitectonic methods. First, the anteromedial and lateral margins were rounded, making the anterior half of the boundary approximately a semicircle. Second, the medial boundary, of a circular form toward the midline, bulged asymmetrically along the emergence of the large vessels (fig. 3, *10 V*) which follow the fissure to supply most of the optically excitable area. This was observed in many experiments other than those recorded here and was one of the observations which prompted the present work. The resultant area was skull shaped rather than circular (dotted line, fig. 3, *9*), the protrusion discussed here forming the jaw of the skull.

Our histologic preparations yielded evidence which correlated with the second finding. The fine granules which characterize the retrosplenial area receded from the line of the fissure toward the midline, both anteriorly and posteriorly (figs. 2 and 3, *7* to *11*). Posteriorly, the medial margin of the optically active area followed the transition zone. Anteriorly, it did not, but curved laterally, to pass across the anterior end of the fissure, typically following for some distance the most anterior of the three large branches which pass laterally from the main vessel of the fissure (fig. 3, *9* to *11*).[7] Thus, the anteromedial margin in our preparations differed from that of Rose in that a wedge of cortex which was not optically excitable extended from the motor area (*Praecag*) posteriorly, between the retrosplenial area (*Rsg β*) and the area parietalis 3 (*Par 3*) and the area striata (*Str*). Likewise, anterolaterally, a similar wedge intervened between the occipital area (*Oc*) and the optically active cortex. The definitive lateral margin of the optically active area extended posteriorly from this wedge, following the zone of histologic transition from *Oc* to *Str* outlined by Rose. The histologic structure of the wedge situated anterolaterally was similar, in our opinion, to that of the area striata (*Str*).

The extent of the excitable area varied somewhat in different rabbits. We have not examined the lateral margin in sufficient detail to say more than that the functional margin as recorded fell within the histologic

7. This distribution of the anterior branch, while typical, is not invariable and therefore does not furnish a reliable landmark for the anteromedial margin of the optically active cortex.

EXPLANATION OF FIGURE 5

Low power photomicrographs (magnified 20 diameters) of three frontal sections, cut at 20 microns and stained by the Giemsa method, illustrating the appearance of areas of the cortex considered significant in interpretation of the physiologic records. The arrows in *13* and *14* indicate the most lateral extent (*c*) of the granules of the retrosplenial territory and the locus (*d*) at which the stratification of the cortex begins to be definitely of the retrosplenial type. *S* shows the position of the fissure. The closed squares and circles designate the positions of points which appear on the plots. *13* is from a frontal section through point *5* of figure *3*, *10*. The section shown in *14* passed through the row of points perpendicular to the median plane in figure *2*, *8*. In *15*, points *5* and *6* + *7* correspond to points *5* and *7* shown in figure *2*, *7*. Point *1* in figure *2*, *7* is likewise entered in *15*, though the stab wound occurred in a more posterior section. The Roman numerals in *15* designate the cortical layers of the area striata.

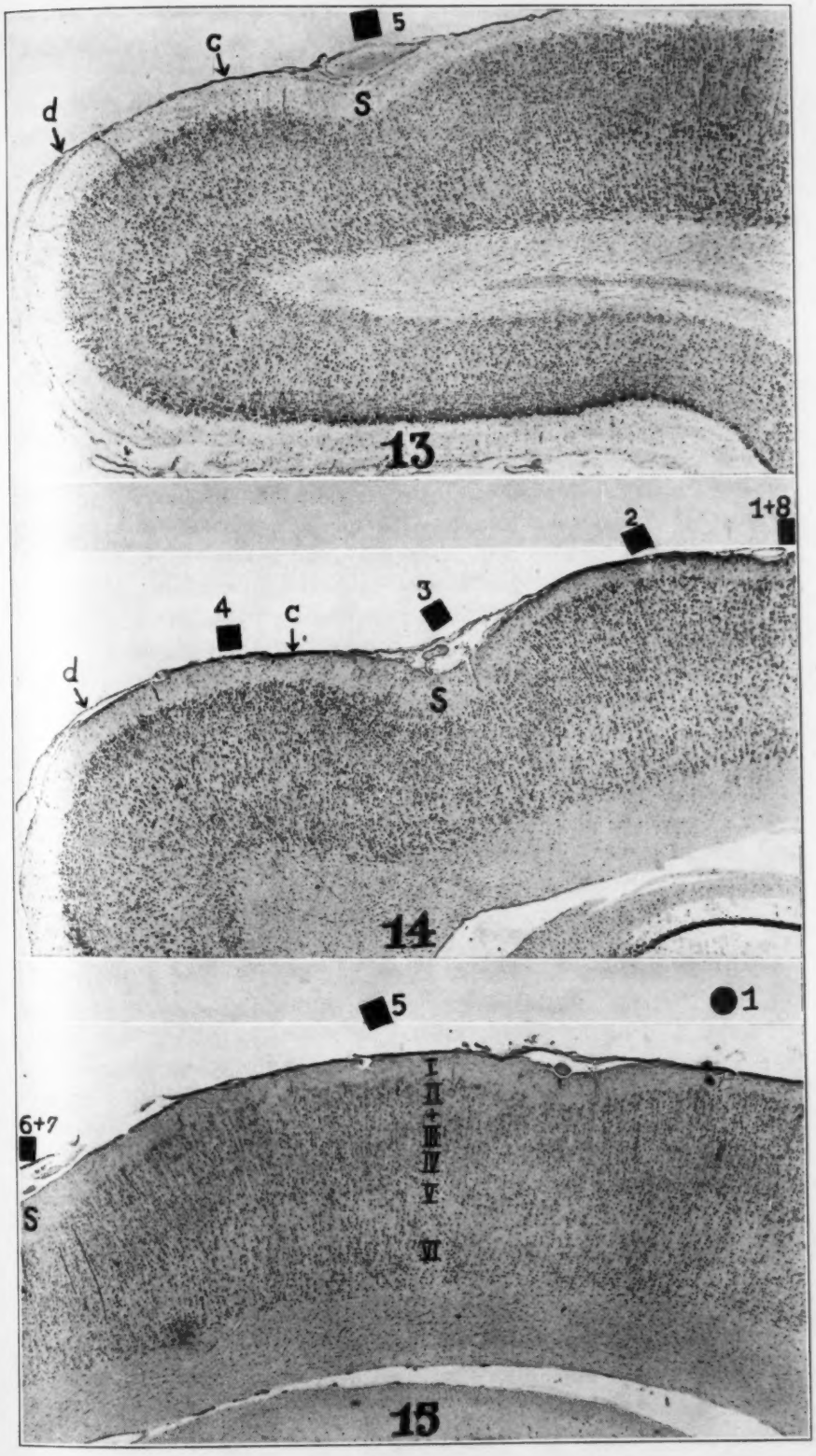

Figure 5.

zone of transition from *Oc* to *Str*. Medially again, it fell in general within the transition zone, definitely medial to the first appearance of the fine granules which characterize *Rsg β* but lateral to the region in which *Rsg β* assumes its complete architectural characteristics. In 2 cases, however (fig. 1, *2* and *5*), records of low amplitude were obtained approximately to the midline when records across the anterior margin of the striate area showed a sharp limit, indicating that the records obtained medially were significant. In another case, the physiologic limit fell precisely at the fissure, although the typical granules commenced at the usual region, about 1 mm. medial to this. If our experiments are reliable (and we have no internal evidence that they are not), in the first 2 cases mentioned an area which appeared histologically to be retrosplenial also received optic projection fibers, and in the third case an area which appeared histologically to belong within the zone of transition from the optic cortex did not. This suggests the possibility that the optic projection area is distinguishable from the cytoarchitectonic striate area. Certainly, in the majority of cases the area labeled peristriate, medial to the striate area of Rose's charts, was optically excitable, and the region along the fissure might give a record approximately as high as that from the central striate region (fig. 1, *2* to *4* and page 491) and indistinguishable from it in form. The amplitude of the record at the fissure was not more reduced, as compared with the central area, than might be inferred from the thinning of the cortex beneath the fissure (fig. 5, *13* and *14*).

The posterior margin was typically found at the posterior pole of the cortex, which corresponded with the usual architectonic demarcation, but in some cases the margin fell anterior to the pole from 2 to 3 mm. For example, a comparison of the records for points *B*, *C* and *D* (fig. 2, *7*) shows that the response was maximal for point *B*, two-thirds maximal for *C* and absent for *D*; giving a sharp margin between *C* and *D*. In this case, line *e* fell at the last section through the posterior pole of the cortex; it was not possible, however, to identify the posterior extent of the area striata, since the cortex was rapidly curving through points *C* and *D* and, consequently, the relations of the layers were disarranged. In the atypical cases in which the posterior margin of the active cortex did not extend to the posterior pole of the cortex, the anterior margin was found more anterior than the branch previously mentioned (page 493) as issuing from the blood vessel of the fissure at this point. This suggests the possibility that an area of constant dimensions could be shifted with some latitude in the antero-posterior dimension.

Histologically, the transition at the anterior margin of the area striata was so gradual that in sections cut in a frontal plane, which did not afford an opportunity for comparison of *Par 3* and *Str* in the same

section, an approximately exact limit could not be obtained. However, the records of activity fell off abruptly to zero when a series of points were measured on a parasagittal plane extending from the anatomic center of the area striata through the anterior margin (fig. 2, 7 and 8; lateral insets). The decline in activity usually occurred in the transition zone of Rose labeled *Par 3 + Str* (indicated in his plate 10, section 738), but in atypical cases the excitable area sometimes extended into *Par 3*.

The form of the record typically obtained from the optically active area after single maximal shocks to the optic nerve is shown in figure 4. It was found to consist of two parts: a quick diphasic wave, lasting about twenty thousandths of a second, and a slower triphasic series, occupying a tenfold period. These were superposed on whatever spontaneous activity the cortex exhibited. The diphasic process has been inferred to signalize the specific visual response, and the triphasic process, activation by the same stimulus of a coordinating or integrating mechanism of the cortex (Bartley, O'Leary and Bishop[8]). The latter is apparently the same as the mechanism which is active spontaneously in the alpha rhythm. In measurements of the records obtained here, when one measurement only is given it is the amplitude of the third wave of the triphasic response, which is the most prominent feature of the record. When three measurements are given, they are: first, the amplitude of the first, surface-positive spike of the diphasic process, with which is summed the start of the first wave of the triphasic process, a much lower element; second, the amplitude, below the base line, of the second, surface-negative wave of the triphasic process, and, third, the third wave of this process, as in the single measurements.

The significance of this information for the present study is as follows: With exceptions to be noted, the amplitudes of the waves of these two processes varied together as the recording electrode was moved across an area of varying activity. Therefore, each was equally characteristic of the optic projection area. They varied, further, parallel to the amplitude of the spontaneous alpha rhythm of the optically excitable area, although this feature was complicated by the fact that adjacent areas also showed spontaneous activity which was not always sharply different from that of the optic area. In some cases, especially across the medial margin, an exception occurred in that certain elements of the response were differentially altered. Either the third wave of the triphasic process, on which several minor peaks were often inscribed, was reduced to a series of diphasic ripples across the base line, as if the main wave had disappeared and only its secondary peaks

8. Bartley, S. H.; O'Leary, J. L., and Bishop, G. H.: Differentiation by Strychnine of the Visual from the Integrating Mechanism of the Optic Cortex of the Rabbit, Am. J. Physiol. **120**:604-618 (Nov.) 1937.

remained, or in some cases the whole complex disappeared, leaving the second, surface-negative wave. The meaning of this unusual picture is not clear, but it appears to represent a successive failure of the elements of the response, starting with the latest component. At any rate, if the earlier elements represent the specifically visual process, it follows that the projection area for afferent fibers extends to the limits of the optically excitable region and that no marginal zone which is activated secondarily by the region receiving the optic radiation can be detected by our technic. If there is a peristriate area in the rabbit brain, it therefore usually differs functionally from the striate area in degree and not in kind and, when differing at all, must lack the auxiliary mechanism involved in visual reception rather than that concerned in projection of sensation. The differences to be observed at the margins were so gradual as to give no criterion for specific demarcation, and the optically excitable area actually encroached medially on the transitional zone containing the beginning of the fine granules which characterize the retrosplenial cortex. Finally, these functional differences occurred not in the region in figure 2, *6* designated as the peristriate area but in the area of transition between this and the retrosplenial field proper. In other words, we could find no functional or histologic justification for differentiating in the rabbit cortex the peristriate and the striate area. In this connection, it may be noted that the stria of Gennari is not obvious in the striate area of the rabbit and that the area is termed "striate" by analogy with the corresponding area of other mammals.

The other obvious consideration that might compromise the accurate determination of the functional margins is the homolateral representation of the uncrossed tract. The effect homolaterally of stimulation of the optic nerve was slight, and the distribution of the response was not conspicuously different from that of the opposite side. Certainly, the field of homolateral activation was not more extensive than that of the contralateral effect, and so would not be expected to complicate the observations reported.

SUMMARY

With 15 rabbits, the extent of the optically active cortex was studied by recording the characteristic interruptions of the spontaneous rhythm which followed the application of single maximal electrical shocks to the contralateral optic nerve. Identifying stabs were placed to locate the points measured in frontal sections cut at 20 microns each and prepared subsequently for histologic control.

Comparisons were made between the extent of the optically excitable area in our histologic preparations used as controls and that of the area striata as delimited in the Rose [3] cytoarchitectonic parcellation of the cortex of the rabbit. The optically excitable area is more extensive

than the area striata as delimited by Rose in that it extends across the peristriate field (*Pstr*) medially and may enter area parietalis 3 anteriorly. Laterally, it follows Rose's zone of transition between the striate (*Str*) and the occipital (*Oc*) field to the posterior pole of the hemisphere. It is roughly round, with an asymmetric bulge at the posteromedial angle, where the large vessels that supply the optically active cortex enter the fissura sagittalis lateralis. The decline in the height of response occurs gradually from a central area of maximal effect toward the margins. At the anterior, medial, lateral and posterior margins it has been shown to fall off abruptly to zero. The field of homolateral activation is of similar dimensions, but the height of response is significantly less.

EFFECT OF LESIONS IN THE VESTIBULAR PART OF THE CEREBELLUM IN PRIMATES

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Comparative neurologists have shown that in amphibia, reptiles and mammals there is a fundamental division of the cerebellum separating a caudal, primarily vestibular, part from a rostral part which receives predominantly spinocerebellar, and in mammals pontocerebellar, fibers (Larsell [1]). Ingvar [2] showed that vestibular root fibers terminate in the cat in the homolateral flocculus and the nodulus and, together with spinocerebellar fibers, in the uvula and lingula. In a previous publication these observations were confirmed in large part, and in addition it was demonstrated that in the rat secondary vestibulocerebellar fibers end bilaterally in the same lobules (Dow [3]). The efferent fibers from these lobules were also observed to be directly connected with the vestibular nuclei, and these efferent connections have recently been demonstrated in Macaca mulatta as well. There is no doubt, moreover, that the afferent and efferent connections of both the paraflocculus and the pyramis are quite different. These parts are not primarily vestibular and have no direct connection with the brain stem.

Except for evidence in the work of Simonelli,[4] Ingvar [5] and Bremer,[6] the literature contains no experiments which differentiate the vestibular parts of the "posterior vermis" from the more dorsal spinal

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1. Larsell, O.: The Cerebellum: A Review and Interpretation, Arch. Neurol. & Psychiat. **38**:580-607 (Sept.) 1937.

2. Ingvar, S.: Zur Phylo- und Ontogenese des Kleinhirns, Folia neuro-biol. **11**:205-495, 1918.

3. Dow, R. S.: The Fiber Connections of the Posterior Parts of the Cerebellum in the Rat and Cat, J. Comp. Neurol. **63**:527-548, 1936.

4. Simonelli, G.: Sulla funzione dei lobi medi del cervelletto: I. Lobe posteriore (pyramis, uvula, nodulus, secondo Ingvar), Arch. di fisiol. **19**:447-478, 1921.

5. Ingvar, S.: On Cerebellar Localization, Brain **46**:301-335, 1923.

6. Bremer, F.: Le cervelet, in Roger, G. H., and Binet, L.: Traité de physiologie normale et pathologique, Paris, Masson & Cie, 1935, vol. 10, no. 1, pp. 39-134.

part. Ferrier and Turner [7] described the effects of lesions of the vermis in monkeys, including those in an animal in which the "posterior part of the vermiform process" was extirpated. Magnus [8] pointed out that all the vestibular reflexes studied by him are present in animals after total removal of the cerebellum. Pollock and Davis,[9] Bauer and Leidler,[10] Groebbels [11] and others have presented evidence that the cerebellum tends to inhibit vestibular reflexes and that after certain cerebellar lesions a release of vestibular reflexes occurs. The effects of lesions of the nodulus and uvula on vestibular reflexes have not previously been studied.

METHODS

This report is based on a study of 19 rhesus monkeys (Macaca mulatta) and 1 of each of the following species: Cercopithecus pygerythrus aethiops (green monkey), Cercocebus torquatus atys (mangabey), Papio papio (baboon) and Pan satyrus (chimpanzee). In 15 of this group primary extirpations of the nodulus and lower part of the uvula were made. In 5 of these animals extirpations were either restricted to one side or involved one side more than the other. The remaining 8 animals were employed for operations as controls, including extirpations of various other lobes of the cerebellar vermis and opening the fourth ventricle and elevation of the vermis without extirpation of tissue, both before and after extirpation of the nodulus and lower part of the uvula. Serial sections were made through the entire vermis of 12 animals; 9 of the animals were killed and the lesions examined grossly; the remaining 2 animals are still alive. In only 1 animal was there any significant injury of the cerebellar peduncles, including the juxtarestiform body, or the adjacent structures of the medulla. In this case the postoperative symptoms were essentially different from those to be described, and the experiment is not included in this report.

All the operations were carried out with the technic outlined by Fulton and Keller.[12] Sodium amytal, pentobarbital sodium or ether was used for anesthesia. After exposure of the cerebellum by a suboccipital approach, the fourth ventricle was opened and an oval wire loop, the width of the vermis and about 1 cm. in length, was passed into the fourth ventricle beneath the posterior vermis.

7. Ferrier, D., and Turner, W. A.: A Record of Experiments Illustrative of the Symptomatology and Degenerations Following Lesions of the Cerebellum and Its Peduncles and Related Structures in Monkeys, Phil. Tr. Roy. Soc., London **185B**:719-778, 1894.

8. Magnus, R.: Körperstellung, Berlin, Julius Springer, 1924.

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10. Bauer, J., and Leidler, R.: Ueber den Einfluss der Ausschaltung verschiedener Hirnabschnitte auf die vestibulären Augenreflexe, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **19**:155-225, 1912.

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12. Fulton, J. F., and Keller, A. D.: The Sign of Babinski, Springfield, Ill., Charles C. Thomas, Publisher, 1932.

By bringing the loop upward and backward it was possible to extirpate the nodulus and lower part of the uvula with little bleeding and without injury to surrounding structures. As the lesion could not be inspected, complete extirpation was not always secured. Lesions restricted to one side of the nodulus and lower part of the uvula were made in the same way, except that the loop in these cases was one-half the width of the vermis. This loop was found useful in making isolated lesions elsewhere in the vermis.

The animals were examined at frequent intervals during a postoperative period of from eight days, in the case of 1 monkey, to several months in the case of others. They were subjected to as complete a neurologic examination as possible. The swimming ability and performance on vertical and horizonal bars were observed when the animals were blindfolded and after this blindfold had been removed. In some monkeys postrotatory nystagmus was studied before and after operation, and in each animal particular attention was paid to tests for vestibular reflexes. Moving pictures were taken of some of the animals.

RESULTS

Symmetric Ablation of the Nodulus and Lower Part of the Uvula.—When the nodulus and lower part of the uvula had been extirpated, the monkeys after recovery from anesthesia frequently fell to one side or the other, and at times forward and backward. The backward falling was much less frequent than after ablation of the pyramis, uvula and nodulus in lower mammals. The monkeys soon avoided moving about and clung tenaciously to the walls of the cage. When they were frightened or attempted to move about, the head, and frequently the whole trunk, oscillated from side to side or in an anteroposterior direction. This movement was at times of such amplitude that it caused the animal to strike its head forcibly against the wall of the cage. If the animal was allowed to be on the floor or if it was placed in a cage with a smooth floor and walls all the symptoms were accentuated. When on the floor the monkey made a few hesitant steps forward with a sprawling, abducted gait until some object could be grasped or it could brace itself in a corner. Once in a stable position, the animal resisted all efforts to dislodge it.

Nystagmus was seen for a few hours after operation in exceptional cases. When the trunk was supported movements of the individual extremities in feeding and in the placing and hopping reactions were executed without any abnormality of movement. There was no change in the deep reflexes or in the resistance to passive manipulation of the extremities.

The first signs of recovery were noticed within two or three days. As walking improved the animals usually deviated toward one side or the other when placed in a narrow corridor. Marked improvement had usually occurred by the end of the first week, and at this time the animals could walk about without falling. Side to side oscillations of

the head and trunk, titubations in walking and a tendency to cling to objects for support were still obvious. All the signs of instability continued to be accentuated when the animals were observed on a flat surface.

An increase in the positive supporting reaction (Stutz reaction) was observed in a few animals for one or two days. In 1 animal this was restricted to the anterior extremities. In another swimming ability seemed to be impaired, but subsequent examination of this animal and of others in various stages of postoperative recovery failed to disclose any consistent defect in swimming ability. Certainly, these animals were as capable of righting themselves when placed in the water blindfolded as were normal monkeys.

Detailed examination of many of the animals failed to reveal any significant changes in the threshold, intensity or duration of postrotatory nystagmus after ablation of the nodulus and lower part of the uvula. Even small differences in the duration of nystagmus, depending on the direction of rotation, observed before operation, were preserved after the lesion. Care was taken to test the animals minimally in order to avoid a habituation effect.

Recovery continued over a period of from three to seven weeks, depending on the completeness of extirpation of the nodulus and uvula. After the period of recovery no abnormality of posture or movement could be detected. One of the last things to reappear after this lesion was the ability of the monkey to walk on a narrow horizontal bar when blindfolded. One animal learned to progress the length of the bar early in postoperative recovery by keeping the chest and abdomen in touch with the bar and dragging itself along. When it attempted to walk, however, it fell, as did all the other monkeys—for as long as seven weeks after operation in some cases.

After ablation of the nodulus and lower part of the uvula the monkeys did not leap about the large wire enclosure in which they were examined. All normal monkeys made frequent long leaps, but for periods of from fifteen to forty-six days, depending on the completeness of the extirpation, the experimental animals could not be induced to make a leap of 5 feet (152 cm.), even when by such a leap they could avoid capture.

Many of the animals were blindfolded and observed as they slid down an inclined plane, feet first, in a lateral position. During the acute stages of the disequilibration animals subjected to this test were often observed, on reaching the floor after sliding about 3 feet (91 cm.), to lurch and sometimes fall toward the inclined plane in a direction opposite that in which the momentum was carrying them.[13] A normal

13. Dr. Léon Ectors first made this observation.

monkey subjected to such a procedure on first trial always adjusted the extension of the extremities to counteract perfectly the momentum of the body and, without any noticeable swaying to either side, immediately walked away. A bilaterally labyrinthectomized animal did not have any reflex extension of the extremities under these conditions and always fell away from the inclined plane as a dead weight; at times it rolled completely over away from the plane. This suggests a possible explanation for this syndrome, namely, an overreaction to a vestibular stimulus or, if one may use the term in this sense, "hypermetria" of vestibular reflexes. Although the reaction was not obtained at every trial, it occurred with sufficient regularity to merit mention. The refractoriness of rhesus monkeys to tests of this character is well known to all who have worked with this species. Such tests when applied to monkeys are always quickly modified by "voluntary" activity, which often interferes in a marked degree with the study of the reflexes.

The syndrome in the baboon was less severe and less enduring and in the chimpanzee, although definitely present, was even more fleeting. A protocol for a monkey (Macaca mulatta) has been selected to show that removal of a minimal amount of cerebellar cortical tissue will produce the syndrome. When extirpation of the nodulus and uvula was more complete the syndrome was identical, though more persistent. In some instances, when extirpation of the nodulus and uvula was complete the lesion involved to a greater or less extent one or both fastigial nuclei. This did not change the syndrome as described except that in these animals the increase in the positive supporting reaction was more noticeable. A protocol for the chimpanzee "Tim" is also given.

EXPERIMENT 1.—*Subtotal ablation of the nodulus and caudal quarter of the uvula in a macaque; oscillation of the head and trunk, falling, titubating abducted gait, reluctance to move, clinging to the wall; gradual compensation in forty days; animal killed; histologic analysis.*

The animal was an adolescent male monkey (Macaca mulatta), weighing 3.1 Kg. It was moderately tame and could be examined easily. The gait was normal.

Operation (Sept. 10, 1936).—With anesthesia induced by sodium amytal and the usual "cross bow" cerebellar exposure, the cisterna magna was opened and the roof of the fourth ventricle exposed posteriorly. The region of the nodulus was ablated with a small wire loop the width of the nodulus itself. The strip of tissue removed included the lower part of the uvula. As there was no bleeding, the wound was immediately closed.

Postoperative Course.—Three hours later the animal had begun to awaken. It showed gross ataxia of the head and trunk, with marked side to side oscillations. It was seen to fall backward twice. There was constant horizontal nystagmus, with the quick component to the right.

Six Hours: The animal was up on all fours and was moving about its cage. There was no tremor in individual movements of the extremities. The monkey stood on a wide base and showed marked swaying from side to side. The tendency to fall backward was still present. The nystagmus continued. The animal was still obviously under the influence of the anesthetic.

First Day: There was marked ataxia of movements of the entire body. When the trunk was well braced, fine movements of the extremities were well executed, without any trace of cerebellar ataxia or tremor. The animal stood with the extremities widely abducted and was seen to move about the cage but little. It usually either clung to the wall of the cage with all extremities or rested in one corner with back braced against the wall. It was able to walk across the floor with a sprawling gait, punctuated with irregular sudden bursts of activity. It fell frequently, but in no particular direction. The falling movements appeared to be initiated in the head and were at times only severe exacerbations of the oscillations of the head and trunk. There was no nystagmus.

Second Day: The symptoms already described continued without any sign of improvement. The animal was less active and resisted all efforts to dislodge it from a well supported position.

Third Day: The animal showed some improvement. It occasionally fell forward on its face, especially when it made a hurried movement or was frightened. It clung tenaciously to any available object for support. The spontaneous side to side oscillations had almost disappeared. There was no nystagmus and no signs of a lesion of any of the cranial nerves. The deep reflexes were active and equal. Fine movements of the extremities were executed perfectly and without tremor.

Fourth Day: The symptoms were essentially unchanged, with perhaps slight improvement. When the animal was allowed to run down a long corridor it showed a tendency to deviate to the left.

Fifth Day: Recovery seemed more rapid in this monkey than in animals with complete removal of the nodulus and lower part of the uvula. It continued to move cautiously and used climbing progression when possible.

Seventh Day: The condition was essentially unchanged. The deviation to the left continued.

Eleventh Day: When the animal was seen in ordinary cage activity no obvious defect was noted. When frightened or forced to make a hurried movement the side to side oscillations were brought out. It continued to use an abducted gait, but no deviation to the left was now noticeable.

Fifteenth Day: The animal was seen to leap once from one wall of the cage to another, a distance of 5 feet (152 cm.), but was still cautious in its movements. It was definitely slower than normal in its ability to escape by climbing about.

Twenty-Fifth Day: The animal showed little abnormal behavior until exhausted; then there was recurrence of the titubations in walking, together with abducted gait.

Thirty-Ninth Day: On careful examination no defect could be detected in posture, movement or reflexes.

Fortieth Day: The animal was killed on October 20.

Observations at Autopsy.—No abnormalities were observed in the heart, lungs or abdomen. No sign of infection was seen about the wound. Examination of the cerebellum revealed superficial bruising of the medial part of the lobulus ansiformis and the lobulus paramedianus, with a slight adhesion to the left part of the pyramis. Midsagittal section of the vermis showed that the inferior half of the nodulus had been removed, leaving two folia intact on the surface next the uvula. The inferior one fourth of the uvula was gone, leaving the rest of the vermis grossly undamaged.

Serial sections stained by the Kulschitsky method revealed that the lesion involved only the folia seen to be damaged when the brain was examined grossly.

The lesions of the lobulus ansiformis and lobulus paramedianus were not significant and could scarcely be distinguished in the sections. The lesion of the pyramis involved only the cortex exposed to the dura. The proportion of the nodulus and uvula which was removed coincided with that described on gross examination. Normal cerebellar cortical tissue separated the lesion from the deep cerebellar nuclei and the peduncles of the cerebellum. The floor of the fourth ventricle was not damaged. The extent of the lesion is shown in figure 1.

Fig. 1.—Diagram showing the extent of the lesion in experiment 1. Note the normal cortical tissue separating the borders of the lesion from the deep cerebellar nuclei and the cerebellar peduncles.

In this figure and in figure 6, the following abbreviations are used: *L. P. MED.* indicates the lobulus paramedianus; *NOD.*, the nodulus; *NU. FAST.*, the nucleus fastigii; *NU. INT.*, the nucleus interpositus, and *UV.*, the uvula.

EXPERIMENT 2.—*Subtotal ablation of the nodulus and uvula in chimpanzee "Tim"; oscillations of the head and trunk; falling, titubating abducted gait; accentuation of unsteadiness of posture and gait in the upright position; clinging to the wall, reluctance to move and deviation to the left; rapid compensation during the first fourteen days; complete recovery in forty-one days; animal killed; autopsy.*

The animal was an immature male chimpanzee ("Tim"), weighing 12 Kg. It was tame and could be examined easily. Neurologic examination before operation revealed no abnormalities of posture or movement.

Operation (Dec. 15, 1936).—With the animal under anesthesia induced by intraperitoneal injection of 9 cc. of a 5 per cent solution of pentobarbital sodium, a cutaneous incision was marked out with the transverse limb extending from one mastoid process to the other, slightly above the superior nuchal line of the occipital bone. The vertical limb of the "cross bow" incision occupied the midline, from the transverse incision to the spine of the seventh cervical vertebra. Subperiosteal reflection following incision along the superior nuchal line, together with a midline incision of the dorsal muscles of the neck, gave adequate exposure of the occipital bone. Two burr holes were then made just below the lateral sinus on either side. These were enlarged with a rongeur until the lateral sinus was exposed, and the occipital bone to the posterior rim of the foramen magnum was removed. The dorsal arch of the atlas was removed. A cruciate incision of the dura mater adequately exposed the posterior surface of the cerebellum and the dorsal surface of the medulla. With great care, the tonsils, which almost obscured the posterior surface of the uvula, were retracted laterally, exposing the lateral surface of the uvula and nodulus. The choroid plexus was seen immediately ventral to the nodulus. The loop of the bovie apparatus was passed to the base of the paramedian sulcus on the right. By working this relatively blunt instrument laterally, it was possible to remove the uvula and nodulus without hemorrhage from the choroid plexus or the posterior inferior cerebellar artery. No cerebellar vessels were clipped or coagulated. The dura was closed in the midline, but not laterally. The deep tissues and the skin were closed with interrupted black silk sutures. The edges of the skin were approximated with a continuous subcuticular stitch.

Postoperative Course.—Seven Hours: The animal was still drowsy from the effects of the anesthetic. It was able to assume a posture on its haunches, with the arms braced in front and widely abducted. There was marked swaying of the entire trunk and head from side to side, even when the animal was not disturbed.

First Day: There was slight side to side and anteroposterior swaying of the head and trunk when the animal sat in its cage. This swaying was especially marked in the brief intervals when it released its hold on the walls of the cage. It was unable to walk about the cage without falling, although movements of the individual extremities were entirely without cerebellar ataxia. There was no nystagmus.

Second Day: The animal moved cautiously about the cage. When it was induced to walk on the hindlegs there was an increase in the unsteadiness, and the legs at times failed to support the weight adequately. When allowed free, it walked with widely abducted limbs and a tendency to deviate, and at times to fall, to the left.

Third Day: Dr. John F. Fulton examined the animal and made the following note: "There is no doubt that the lesion made in the roof of the fourth ventricle, involving the nodulus and part of the uvula on the right side, has

produced a syndrome strikingly similar to that produced in young children by midline tumors arising from the roof of the fourth ventricle. The animal exhibits the same cautiousness in movement, sitting on a broad base, holding itself up with one arm and grasping the bars of the cage, with occasional slight swaying but with no tremor of the extremities. The syndrome was most conspicuous the first and second days after the operation, but is still present in a fairly marked form."

The animal was unable to maintain its position on a narrow ledge 1½ inches (3.8 cm.) wide.

Fourth Day: The animal was able to walk upright if one steadied it by holding its hand. There was an increase in the unsteadiness, however, as compared with that when it was allowed to walk on all fours. When it was free it progressed cautiously and usually walked along a wall or where it could grasp something for additional support.

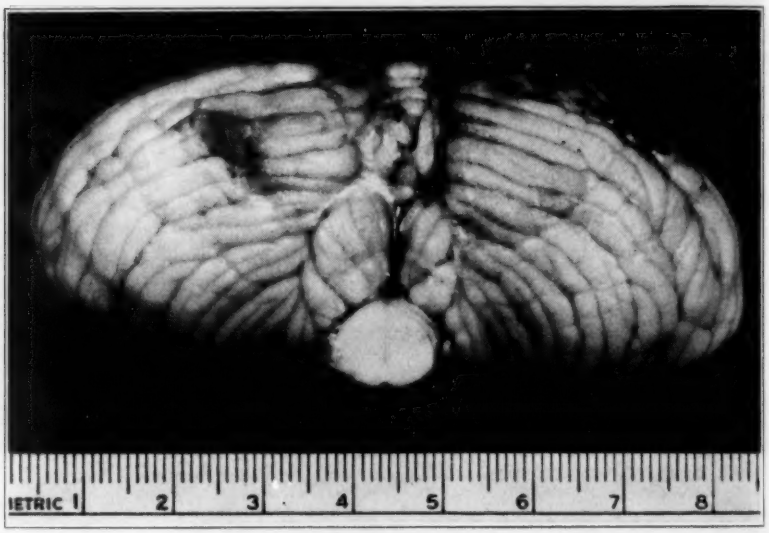

Fig. 2 (experiment 2).—Posterior surface of the cerebellum of chimpanzee "Tim." Note the intact tonsils and upper part of the vermis. Lesions seen on the hemispheres were produced during stimulation at the time that the animal was killed.

Fifth Day: The animal continued to improve, but still walked slowly with a wide base. It was usually seen grasping the walls of the cage for additional support and was still unable to maintain its balance on the narrow ledge. It could stand on its posterior extremities, however, and secure food placed on the top of the cage. This caused an increase in the symptoms of unsteadiness.

Eighth Day: Continuous improvement had been noticeable during the preceding three days. There was no deviation to the left in walking. The animal could stay on the ledge of the sink for short intervals, though it obviously was unsteady. In this position it showed moderate swaying of the head and trunk.

Eleventh Day: Because the animal continually picked at its wound, a superficial infection of the skin resulted. The neurologic status continued to show improvement. The cage activities seemed normal, although the animal was still

retarded and cautious in its movements. When it was placed on a narrow ledge there were trembling of the legs, instability of the trunk and swaying, and it invariably fell if left entirely unsupported.

Seventeenth Day: The animal was examined by Dr. John F. Fulton, who observed that the syndrome was much less conspicuous than one week previously. There was much less swaying and titubation, but the animal was still cautious in its movements, especially when walking along the edge of the sink or on a narrow rail.

Twenty-Ninth Day: The general condition of the animal was good. No defect could be detected in its activity as seen in the cage. Ability to walk along a narrow ledge had improved since the last test; although the animal objected to the procedure and showed some titubation, it was able to sit on the bar unsupported without falling.

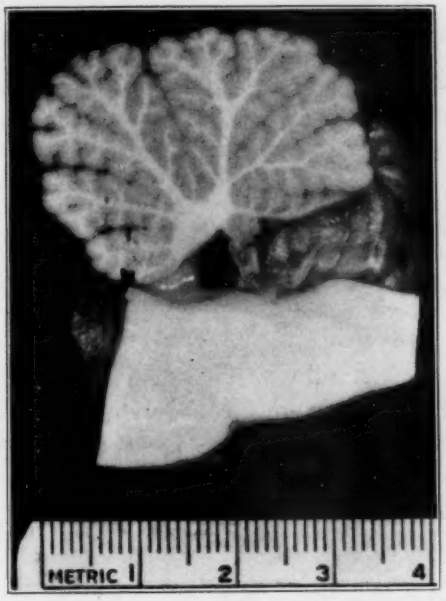

Fig. 3 (experiment 2).—Midsagittal section through the cerebellum and lower portion of the brain stem of chimpanzee "Tim."

Forty-Sixth Day: The general condition of the animal was excellent. The weight was 14 Kg. No defect in any activity could now be observed. The animal walked on the narrow ledge like a normal chimpanzee and was not confused or frightened in the slightest by the procedure.

Second Operation (Fifty-First Day, February 5).—A strip lesion of the posterior part of area 4 was made on the right side, and the right oculomotor nerve was sectioned. After this operation there developed osteomyelitis of the skull.

Third Operation (One Hundred and Sixty-Second Day, May 26).—Stimulation and extirpation of area 8 on the left side and repetition of section of the right oculomotor nerve were carried out.

May 27: The right cerebellar hemisphere was stimulated. The animal was killed.

Autopsy.—No abnormalities of the heart, lungs or abdominal viscera were observed. The part of the left parietal bone which had been included in the bone flap remained as a flat, thin sequestrum. There was new formation of bone over the dura at this point. There was no extension of the infection subdurally and no sign of infection about the site of operation on the cerebellum. The posterior surface of the cerebellum was undamaged except for slight adhesion of the dura to the lobulus ansiformis on the left side. The tonsils touched in the midline, and the uvula could not be seen (fig. 2). There was no evidence of damage to the medulla. A midsagittal section of the cerebellum revealed that the nodulus was completely ablated except for the most proximal folium. The uvula was entirely removed except for the most superior folia. The choroid plexus was intact, and there was no involvement of the other lobules of the vermis (fig. 3). There was no sign of a lesion in the deep cerebellar nuclei, the cerebellar peduncles or the floor of the fourth ventricle. The cerebellum is now being prepared for histologic examination.

Asymmetric Ablation of the Nodulus and Lower Part of the Uvula.—Although no lesion produced by this method was exactly symmetric bilaterally, in several animals the lesions were restricted to one side of the nodulus and lower part of the uvula or were much more extensive on one side. In 2 experiments, after recovery from extirpation of the left half of the nodulus and uvula, the right half was ablated, with return of the symptoms, although in reversed direction. After excision of the left half, in addition to the syndrome of disequilibration already described, the animals showed rotation of the head with the occiput to the right and the chin to the left. They fell to the right and deviated to the right in running and jumping. They spiraled toward the right about the longitudinal axis of the body in jumping and in climbing a vertical bar. In 2 animals, at one stage of postoperative recovery the deviation in running reversed itself, although the rotation of the head remained as already described. Nystagmus was usually present for several hours and, when seen, was horizontal, with the quick component toward the side of operation. It should be noted that these postures of the head and abnormalities of movement are the reverse of those seen after unilateral labyrinthectomy, in which the head is rotated with the occiput toward the side of operation and the spiraling and deviation are toward the same side. The titubations and oscillations of the head and trunk were less marked in the experiments in which the ablation was restricted to one side than when the lesion was symmetric. The period of recovery was shorter, although the rotation of the head was seen for four or five weeks after operation. The behavior of these animals when placed in the water was quite different from that of unilaterally labyrinthectomized animals. The labyrinthectomized animals rolled in the water and were unable to swim for several weeks after the operation. The cerebellar animals, although they circled toward the normal side and when blindfolded swam in a lateral position on the normal side, were all able to swim, and none were observed to spiral or

roll. No difference in the intensity, threshold or duration of postrotatory nystagmus, depending on the direction of the rotation, could be detected in the animals of this group. There was no difference in the deep reflexes or in the resistance to passive manipulation on the two sides.

EXPERIMENT 3.—*Lesion of the left half of the nodulus and uvula in a macaque; oscillation of head and trunk; titubating, abducted gait; falling to the right; rotation of the head with the occiput to the right; deviation to the right in walking; spiraling to the right in climbing and jumping; gradual compensation, incomplete in fourteen days; animal killed; histologic analysis.*

The animal was an adolescent female monkey (Macaca mulatta), weighing 4 Kg. It was moderately tame and could be examined easily. The posture and gait before operation were normal.

Operation (Jan. 20, 1937).—With the animal under anesthesia induced with pentobarbital sodium, an exposure identical to that in experiment 1 was made. The wire loop was made half the width of the vermis, and the lesion was restricted to the left of the midline. There was no bleeding and the wound was immediately closed.

Postoperative Course.—At the conclusion of the operation there was conjugate deviation of the eyes toward the right.

Six Hours: The animal was still under the influence of the anesthetic, but showed rotation of the head with the occiput to the right and the chin to the left. It fell to the right at every attempt to walk. The eyes showed conjugate deviation to the right, and there was inconstant horizontal nystagmus, with the quick component to the left. The nystagmus was accentuated when the animal looked toward the left. There was less oscillation of the head and trunk than is seen after symmetric extirpation of the nodulus and lower part of the uvula. The falling movements appeared to start as a deviation of the head to the right. They were seen at times when the left forelimb was flexed, or even when it did not touch the floor of the cage; they could not, therefore, be due to an increased supporting reaction in the left forelimb.

First Day: The animal was able to sit up in the cage. The head was rotated as before. In the standing position, the trunk was inclined to the right. The animal fell frequently to the right. When leaping from the examiner's arms to the cage, it spiraled 180 degrees, the back turning toward the right. The animal showed the same tendency to cling to the wall of the cage as was seen after symmetric ablation of this part of the cerebellum. There was no leaping about the cage or nystagmus, and the eyes were no longer deviated.

Second Day: The general condition of the animal was excellent. The neurologic findings were essentially as before. There was no sign of injury to the cranial nerves. The deep reflexes were active and equal on the two sides.

Third Day: The monkey showed considerable improvement in ability to move about in the cage. It was still cautious in its movements and clung constantly to the wall of the cage. It walked on the floor only long enough to reach an object to which it could cling. When it was climbing the defects of posture and movement were less noticeable than when it was on the floor. In running down a long narrow corridor it deviated either toward the right or toward the left. It usually ran along the side of the corridor with the trunk sliding along the wall. There was no nystagmus. There was no difference in the intensity, threshold or duration of postrotatory nystagmus, regardless of the direction of rotation.

Fifth Day: The monkey showed reversal of the tendency to fall to the right, and now was seen to fall and to deviate to the left. The head, however, continued to be rotated with the occiput to the right and the chin to the left. The deep reflexes and the resistance to passive manipulation showed no significant changes from the normal. The movements of the individual extremities had not shown any sign of cerebellar ataxia since the operation.

Eighth Day: The animal continued to improve, although it still clung to the wall of the cage. It did not leap about when allowed in a large wire enclosure. There was some oscillation of the head and trunk during excitement. The rotation of the head continued as before. The monkey was not observed to fall.

Thirteenth Day: The monkey was obviously handicapped in the movements in the cage. When it was frightened or attempted to move quickly, it showed disability in movements of the head and trunk. The animal on several occasions was seen to strike its head forcibly against the bars of the cage. There was no leaping about the small cage or when it was released in the larger enclosure. When placed in the corridor the monkey ran rapidly, but the hind quarters tended to deviate toward the left, and at times to strike the wall of the corridor. The head, however, was rotated as before with the occiput to the right and the trunk inclined toward the right. The animal was unable to walk on a narrow horizontal bar when blindfolded. In attempting to do so it fell, either to the right or to the left. The animal no longer spiraled toward either side when climbing the vertical bar. When allowed to slide down an inclined plane it fell consistently toward the right, regardless of which side was against the board as it slid down. As a result, when the monkey was on its right side the direction of lurching or falling was opposite that toward which momentum would naturally carry it.

Fourteenth Day: The animal was killed.

Autopsy.—No abnormalities were observed in the thorax or abdomen. There was no infection at the site of operation. The cerebellum was grossly intact except for a lesion, 3 mm. in width, involving the left half of the lower folia of the uvula, and a strip of tissue, of the same width, which had been removed from the nodulus on the left side. Serial sections cut transversely through the entire cerebellum and brain stem showed that the lesion was as described grossly. There was slight superficial bruising of the nucleus gracilis on the left side, and several adhesions were present on a few folia of the lobulus ansiformis and lobulus paramedianus. These were all small. There was no damage to the lingula, the deep cerebellar nuclei and the cerebellar peduncles, including the juxtarestiform body and the fastigiobulbar tracts. A detailed description of the degeneration resulting from this lesion is reported elsewhere.[14]

In another monkey, the posteroinferior two thirds of the nodulus and uvula was first extirpated on the left side. This was followed by rotation of the head with the occiput to the right and all the other symptoms previously outlined (fig. 4 *A*). After recovery was complete, the right half of the same lobule was ablated. This was followed by return of all the signs as before, except that they were reversed in direction (fig. 4 *B*). The gross appearance of the lesions on the two

14. Dow, R. S.: Efferent Connections of the Flocculonodular Lobe in Macaca Mulatta, J. Comp. Neurol. **68**:297-305, 1938.

sides are shown in figure 5 *A* and *B*, with which figure *C*, a photograph of a midsagittal section through the normal cerebellum of a Macaca mulatta monkey, may be compared.

Excision of the Nodulus and Lower Part of the Uvula After Bilateral Labyrinthectomy.—The nodulus and lower part of the uvula were removed in 2 monkeys after recovery from bilateral labyrinthectomy. Extirpation of the nodulus was not done until the monkeys had recovered sufficiently to be able to walk and run without falling and without showing any oscillations of the head and trunk. A detailed description of these preparations has been given elsewhere (Dow [15]). After labyrinthectomy these animals were unable to swim when blindfolded or,

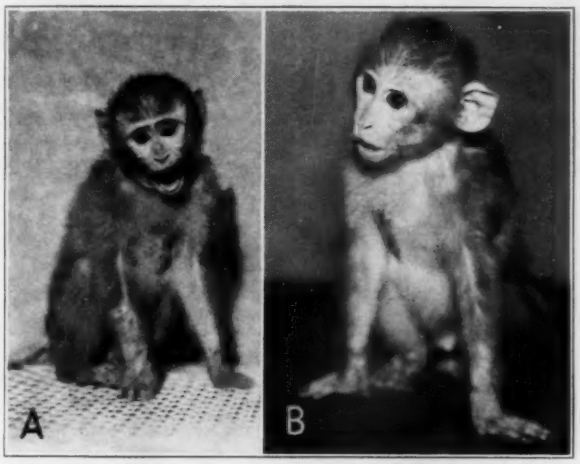

Fig. 4.—*A*, a monkey sixteen days after extirpation of the left half of the nodulus and lower part of the uvula. Note the rotation of the head with the occiput to the right. *B*, the same animal one day after extirpation of the right half of the nodulus and lower part of the uvula. Note that the rotation has become reversed in direction and is now with the occiput to the left.

if once submerged, when the blindfold was removed. They were unable to maintain their balance when placed blindfolded on a narrow horizontal bar. All vestibular reflexes, including postrotatory and caloric nystagmus, were absent. In the case of the animal with simultaneous bilateral labyrinthectomy, it required about two months to arrive at such a stable state of postoperative recovery. In the case of the animal in which the two operations were done separately, less than half this time was required.

15. Dow, R. S.: The Effects of Unilateral and Bilateral Labyrinthectomy in Monkey, Baboon and Chimpanzee, Am. J. Physiol. **121**:392-399 (Feb.) 1938.

In such preparations removal of the nodulus and lower part of the uvula added no sign to the previously existing conditions except a transient increase in the positive supporting reaction. This persisted less than forty-eight hours. There were no side to side oscillations of the head and trunk after the first twenty-four hours following operation. The animals were able to walk across the floor without falling on the

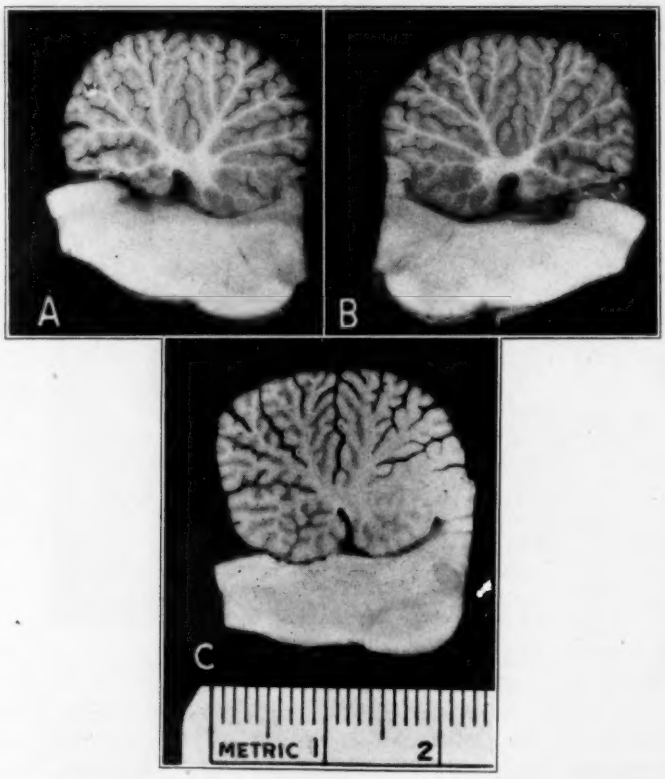

Fig. 5.—*A*, left half of the cerebellum and brain stem of the same monkey as that illustrated in figure 4. Note the extirpation of the lower two thirds of the nodulus and of the uvula. *B*, right half of the cerebellum and brain stem of the same monkey as that shown in *A*. Note the extirpation of two thirds of the nodulus and of the uvula, as compared with the normal brain as seen in *C*. *C*, midsagittal section through the normal cerebellum and brain stem of a monkey (Macaca mulatta).

day of operation. Removal of the nodulus and lower part of the uvula in no way modified the existing symptoms of bilateral labyrinthectomy already described.

Preliminary observations, in work not yet completed, appear to indicate that unilateral extirpation of the nodulus and lower part of

the uvula after bilateral labyrinthectomy is capable of inducing an abnormal posture of the head and a tendency to spiral identical in direction with, and as persistent as, that in the animal with labyrinthine function. Various combinations of destruction of the labyrinth and cerebellar lesions are now being studied.

EXPERIMENT 4.—*Simultaneous bilateral labyrinthectomy; severe disorder of posture and locomotion with gradual compensation, incomplete in two months; permanent loss of vestibular function. Second Operation: ablation of the nodulus and lower half of the uvula; transient increase in the positive supporting reaction, absence of syndrome as seen in previous experiments; animal killed; histologic analysis.*

The animal was an adolescent male monkey (Macaca mulatta), weighing 2.2 Kg. It was moderately tame and could easily be handled. Neurologic examination and careful observation, including that of swimming ability, failed to disclose any defect of posture or movement.

First Operation (Nov. 18, 1936).—Bilateral labyrinthectomy was performed at one operation by an approach through the mastoid process. The details of the procedure have been given elsewhere (Dow [15]).

Postoperative Course.—The details of the postoperative recovery have also been given elsewhere.

Fifty-Sixth Day: Postoperative recovery seemed to be stationary. The animal was able to run about a large enclosure and to climb about the walls of the cage without falling. It was never observed to leap from one wall of the cage to another or to the floor. The head at times assumed bizarre positions in hyperextension and hyperflexion, and at times to one side or the other. The animal was incapable of swimming and showed loss of all vestibular reflexes, including postrotatory nystagmus and absence of caloric response in both ears. It also showed paralysis of the left side of the face and apparently was totally deaf.

Second Operation (Jan. 18, 1937).—With the animal under anesthesia induced with pentobarbital sodium, the nodulus and lower part of the uvula were extirpated as completely as possible, the method described in experiment 1 being used.

Postoperative Course.—Five Hours: The animal was still somewhat under the influence of the anesthetic, but was able to sit up and walk about the cage. When the door of the cage was opened, it was able to climb out of the cage and walk across the floor, a distance of 10 feet (300 cm.), without falling. The legs were used in a somewhat hyperextended position, and there was an increase in the positive supporting reaction when it was tested by pressure on the trunk, with the animal standing on the floor. There was no side to side swaying, no sprawling gait and no forced movements of any kind.

First Day: The animal was examined carefully, and the contrast between its behavior and that of a normal animal after excision of the nodulus and lower part of the uvula was indeed striking. The labyrinthectomized animal was able to sit up in its cage without grasping the wall for support. There were no side to side oscillations of the head or any swaying of the trunk. When the animal was allowed on the floor there was perhaps a slight increase in abduction and extension of the extremities, but the increase in the positive supporting reaction was not obtained consistently. There was no tremor in the individual movements of the extremities.

Sixth Day: The animal was studied daily after the operation; at no time did it show any of the symptoms which my associates and I were accustomed to

see after extirpation of the nodulus and uvula in an otherwise intact animal. There was no increase in the positive supporting reaction, no increased abduction in gait, no titubations in walking or running and no clinging to the walls of the cage other than that present before the second operation. There was complete absence of the vestibular reflexes. The head continued to be seen in bizarre postures. In short, the condition could in no way be differentiated from that prior to the cerebellar lesion.

Fig. 6.—Diagram showing the extent of the lesion in experiment 4. Note that the lesion here is larger than that in experiment 1 (fig. 1).

Twenty-Ninth Day: Careful studies during the period by several observers revealed no change in the condition from that already reported.

Autopsy.—After ether anesthesia, physiologic solution of sodium chloride followed by a 4 per cent solution of formaldehyde, made neutral, was injected into the circulatory system. The brain was removed at once and was placed

in a solution of formaldehyde of the same concentration. There were no signs of infection at the site of any of the previous operations. There were fine adhesions between the lungs and the costal pleura and a few tiny tuberculous lesions of the spleen and liver. There were no signs of consolidation or cavitation in the lungs. The rest of the examination revealed no abnormalities.

The posterior surface of the cerebellum was slightly adherent to the overlying dura at the most posterior border of the uvula. The remainder of the folia appeared grossly undamaged. Midsagittal section of the cerebellum and brain stem revealed that the extirpation included the entire nodulus and the inferior two thirds of the uvula. There was no gross evidence of any damage to the deep cerebellar nuclei, and no adhesions resulting from the lesion of the fourth ventricle were seen. Examination of the site of labyrinthine extirpation on the left showed that the vestibule was filled with a mucoid material and that it opened into the middle ear. The right vestibule was not dissected, but was sent with the left for serial section.

Histologic Examination.—The cerebellum and brain stem were cut serially in a sagittal plane and stained by the Kulschitsky technic. The microscopic characteristics of the lesion corresponded with the gross appearance. The lower two thirds of the nodulus and uvula were included. There was no involvement of the floor of the fourth ventricle, and normal cerebellar cortical tissue separated the lesion from the deep cerebellar nuclei and the cerebellar peduncles. Examination of the serial sections through both labyrinths revealed that the cochlea was in large part intact but that the vestibule was destroyed.

In addition to the operations already described, cerebellar cortical tissue was removed from other parts of the vermis. In 1 animal, the lobulus C_2 of Bolk and the medial part of the lobulus simplex were ablated. In another, the same lobules and the medial part of the culmen were extirpated. In 3 monkeys the pyramis was ablated—in 2 as a primary operation and in 1 after recovery from a lesion of the nodulus and uvula. The syndrome described as occurring after extirpation of the vestibular parts of the cerebellum was not found in any of these experiments. In all 3 animals in which the pyramis alone was damaged little that was abnormal could be detected, except that the animal when running down a long corridor apparently was unable to stop quickly enough to avoid crashing head-on against the end wall. No visual defect was present. The abnormality was never observed later than the third or fourth day after operation. Extirpation of the pyramis, uvula and nodulus showed no essential difference in effect from extirpation of the nodulus and uvula alone. Ablation of the nodulus and uvula after recovery from extirpation of the pyramis showed no abnormalities which differed from those seen after the same operation done as a primary procedure.

As a further control, in 2 monkeys the fourth ventricle was exposed and the vermis elevated without excision of any tissue. In 1 animal this was done as a first operation, and in another, after recovery from ablation of the nodulus and lower part of the uvula. In the second monkey the hemorrhage and tissue reaction in the fourth ventricle were

at least as severe as those seen in any animal with ablation of the nodulus and lower part of the uvula. In neither monkey was any defect of posture or movement detected after operation.

COMMENT

That disturbances of equilibrium occur after lesions of the posterior vermis has been known for many years. Ferrier and Turner [7] and, most recently, Botterell and Fulton [16] have described the syndrome which follows lesions of the vermis in monkeys. Russell,[17] Rothmann,[18] Ingvar,[2] Simonelli [4] and others described the effects of such lesions in various lower mammals. Prominent among the abnormalities described by most of these investigators, especially in the subprimates, was the frequent occurrence of "forced" falling backward, which gradually disappeared during postoperative recovery. Simonelli [4] observed that backward falling was seen only when the nodulus and uvula were involved in the lesion and never when the pyramis alone was damaged. Ingvar [5] confirmed this and suggested, largely on anatomic grounds, that the vestibular nerve plays a role in the production of the falling movements. Simonelli dismissed the observations as "dynamic phenomena" and expressed the opinion that they have little physiologic significance. He made an observation which we have confirmed in 1 cat, namely, that after complete removal of the pyramis, uvula and nodulus attacks of opisthotonos and falling backward may be induced by extending the head and may be stopped or prevented by forcibly flexing the head.

Stimulation of the nodulus has never been reported on. One may infer from the work of Bremer [6] that the effects on decerebrate rigidity produced by cerebellar stimulation are found after stimulation of the pyramis but not of the more posterior folia of the vermis. He said, after speaking of the inhibition of decerebrate rigidity by stimulation of the anterior lobe:

> This coincidence, certainly significant, of the excitable region with the zone of projection of the spinocerebellar fibers is confirmed by the existence of similar excitability, much more difficult to demonstrate, in the part of the posterior lobe which receives spinocerebellar fibers.

The work presented here indicates that in primates there is a functional division within the so-called posterior vermis. Extirpation of the lower folia and the nodulus and uvula is followed by a syndrome of disequilibration which is not found after extirpation of other parts

16. Botterell, E. H., and Fulton, J. F.: Functional Localization in the Cerebellum of Primates, J. Comp. Neurol. **69**:31, 47 and 63 (Aug.) 1938.

17. Russell, J. S. R.: Experimental Researches into the Functions of the Cerebellum, Phil. Tr. Roy. Soc., London **185**:819-861, 1894.

18. Rothmann, M.: Die Funktion des Mittellappens des Kleinhirns, Monatschr. f. Psychiat. u. Neurol. **34**:389-415, 1913.

of the cerebellar vermis. It is probable that this is a vestibular disorder. This conclusion is supported not only by anatomic evidence but by the fact that the syndrome is not seen after the same lesion if the animal has previously been deprived of vestibular function by bilateral labyrinthectomy.

Although there is abundant evidence to indicate that the nodulus and uvula are primarily in functional relation with the vestibular system, they are not exclusively so. This is shown by the preliminary observation that after recovery of the animal from bilateral labyrinthectomy, an asymmetric lesion of the nodulus and uvula was followed by imbalance of the reflex patterns of posture and movement even in the absence of vestibular function. It is possible that if more time is allowed for recovery from labyrinthectomy, symmetric lesions will induce postoperative symptoms even in the absence of vestibular function.

If the lateral half of the nodulus and uvula was removed, there were, in addition to the syndrome of disequilibration, rotation of the head and deviation and rotation in running, jumping and climbing which were the reverse of those seen after labyrinthectomy on the same side. Ferraro and Barrera,[19] after lesions of the supramedullary portion of the juxtarestiform body, made a similar observation. They concluded that these effects result from interruption of the fastigiobulbar tracts. They may be due to interruption of the direct fibers from the nodulus and uvula to the vestibular nuclei. In fact, in 2 animals in which the lesion of the nodulus and uvula was symmetric but there was unilateral damage to the fastigial nucleus, rotation of the head, spiraling and deviation were not seen. In pigeons, Groebbels[11] found, after unilateral lesions of the lateral nucleus of the cerebellum, head postures and other signs which were the reverse of those caused by labyrinthectomy on the same side. This and other observations made after lesions of the posterior vermis led him to the conclusion that the "posterior vermis" exerts an inhibitory effect on the vestibular reflexes. Both Pollock and Davis[9] and Bauer and Leidler,[10] using different methods, concluded that the cerebellum exerts an inhibitory effect on the vestibular centers. Bauer and Leidler demonstated that the fastigial nucleus is the principal source of this inhibitory influence. Our findings after unilateral lesions of the vestibular part of the cerebellum suggest that these parts inhibit the vestibular centers of the brain stem.

Against this conclusion is the failure to detect any change in the intensity or duration of postrotatory nystagmus after lesions of the

19. Ferraro, A., and Barrera, S. E.: Effects of Lesions of the Juxtarestiform Body (I. A. K. Bundle) in Macacus Rhesus Monkeys, Arch. Neurol. & Psychiat. **35**:13-29 (Jan.) 1936.

nodulus and uvula. Neither does this extirpation affect the symptoms resulting from subsequent unilateral labyrinthectomy.[14] The response to the inclined plane test, an overreaction to a specific vestibular reflex (extension of the extremities to a vertical movement downward), occurred after excision of the nodulus and uvula. This suggests that this syndrome may be a "hypermetric" response to certain vestibular impulses and not necessarily a general release of all the vestibular phenomena. It is certain that there is no loss of any vestibular reflex after this lesion.

This syndrome, produced experimentally, resembles that seen in patients with midline tumors of the cerebellum, particularly the medulloblastomas. According to Bailey,[20] the earliest and most frequent neurologic sign in a patient with a tumor of this type is staggering, unsteady gait. He said: "The trouble in maintaining equilibrium is in striking contrast to the slight ataxia of the extremities when the patient is lying in bed." In fact, this finding plus projectile vomiting, and usually headache, may be the only indications of the tumor in the early stages. Although it was known that these tumors arise from the basilar parts of the cerebellar vermis, Ostertag[21] has shown recently that they originate from the tissue at the base of the nodulus. It must be recognized that such tumors may spread rapidly and usually involve not only the entire vermis but the vestibular nuclei as well.

SUMMARY AND CONCLUSIONS

1. A study of the neurologic disorder in monkeys and chimpanzees resulting from complete and partial ablation of the nodulus and uvula has been made.

2. This is a disorder of equilibration primarily due to vestibular dysfunction. The exact functional disturbance of the vestibular system was not determined.

3. It has been shown that the "posterior vermis" is not a functional entity but that the disorder described is produced only when the nodulus and uvula are damaged.

4. The work indicates that localization of function, based on comparative anatomic facts and afferent fiber connections, may be demonstrated to exist in the cerebellum of monkeys and chimpanzees.

5. The similarity between this syndrome and that seen in cases of cerebellar tumors which originate in this part of the vermis is mentioned.

Dr. John F. Fulton gave assistance and advice throughout this study.

20. Bailey, P.: Intracranial Tumors, Springfield, Ill., Charles C. Thomas, Publisher, 1933.

21. Ostertag, B.: Einteilung und Charakteristik der Hirngewächse, Jena, Gustav Fischer, 1936.

ACUTE AMAUROTIC EPILEPSY IN MACACUS RHESUS

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In 1935 we[1] published a clinicoanatomic study of 5 cases of a neurologic disorder observed in monkeys, Macacus rhesus, in the Zoological Garden of Antwerp, Belgium. In 3 of these cases the termination was fatal, which permitted a complete histologic study of the lesions. We called this disorder "acute amaurotic epilepsy." The syndrome was characterized by awkwardness in movement, epileptiform seizures and disturbance of vision, unassociated with changes in the optic fundi. The duration of the illness was usually from five to eight days, but frequently was only thirty-six hours. It was not always fatal. There were no symptoms referable to dysfunction of the pyramidal system or the peripheral neurons; there was no anemia, digestive trouble or pulmonary complications. Both sexes may be affected, though in our series the females were more often attacked than the males. The cause of the disease is as yet undetermined. Attempts to transmit the condition have failed. No after-effects have been observed to date.

The observations at autopsy were variable and diverse. The essential lesions were parenchymatous degeneration of the vascular type in the occipital, and occasionally in the central, cortex and in the white matter of the occipital and central subcortical regions. In addition, there was extensive macroglial, and sometimes vascular, proliferation in the cortex, independent of the parenchymatous lesions. Frequently, leukocytic infiltration of the meninges, and even of the cortex, were to be seen. Small perivascular nodules bearing a resemblance to those observed in typhus were present.

During 1935 we observed 6 additional cases of this syndrome; in 3 of these the illness terminated fatally, while in the other 3 the animals apparently recovered completely. The tissues of the animals which died were available for detailed histologic study. In 1936 5 more cases

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From the Zoological Garden of Antwerp, Belgium, and the Department of Pathology of the Institut Bunge.

1. van Bogaert, L., and Scherer, H. J.: Akute amaurotische Epilepsie bei Macacus Rhesus. Ztschr. f. d. ges. Neurol. u. Psychiat. **152**:757, 1935.

occurred, in only 1 of which was there a fatal outcome. In the 4 remaining cases recovery was spontaneous, and there were no after-effects.

In this paper it is our purpose to report clinical observations in 7 cases, in 4 of which detailed histologic studies are described. In our first report it was emphasized that the animals became sick during a period between August 23 and October 6, and it is of importance that in the years 1935 and 1936 the same seasonal incidence was found (table 1). One is forced to consider that the season or the type of food specific to a certain period of the year may play a role in this disease. It is not yet possible to draw any definite conclusions as to the cause of the disease.

The histologic observations in the cases occurring in 1935 and 1936 have allowed us to determine the essential pathologic changes in this condition. In addition, it has been possible to describe lesions which were not seen in the animals dying in 1934, for instance, *Strauchwerke* in the

TABLE 1.—*Seasonal Incidence of Acute Amaurotic Epilepsy in Monkeys for the Years 1934-1936* *

Year	January	February	March	April	May	June	July	August	September	October	November	December	Total No. of Cases
1934	..	..	..	..	..	..	..	0	++0	+	..	..	3
1935	..	..	..	..	..	..	..	+	+00	+0	..	..	6
1936	..	..	..	..	..	..	+	0	000	..	..	..	3

* 0 indicates that the animal survived, and +, that the animal died or was killed.

cerebellar cortex and vascular lesions in the cornu ammonis. Lesions similar to the latter can frequently be seen in cases of human epilepsy, but to our knowledge have not been described in monkeys.

CLINICAL DESCRIPTION

In reporting our cases we shall describe the first in detail, as it is typical of a case in which the outcome was fatal. The fourth will also be reported in detail, as typical of that of an animal which recovered. We were fortunate in securing an excellent cinematographic film, which recorded in detail the clinical phenomena observed.

CASE 1.—A female monkey (Macacus rhesus [India]) from 1 to 1½ years of age, had been at the zoo since May 1935. The food consisted of fruit, vegetables and rice.

On Sept. 15, 1935, the animal had two epileptic fits in six hours, after which there was impairment of vision for a short period. On the following morning the animal appeared to have recovered, except for some defect in sight. It was unable to grasp objects and missed the bars of the cage. It was easily excited. In the afternoon of the same day the monkey continued to be restless and the pupils were fixed; vision was not completely lost, for it drew back on the approach of a hand. No more fits were observed. On September 17 it was

observed that the animal had taken refuge on a bar of the cage, and that the eyes were wide open. The pupils appeared to be of normal size. A hand passed in front of the eyes caused no blinking, and when the animal attempted to get down from the perch it was unable to find the bars readily. It was apparently blind. At 9 a. m. there was recurrence of fits at short intervals. The animal kept turning to the left until it dropped to the ground. Blindness continued. At 11:30 a. m. the fits ceased, leaving the animal in a state of prostration, with the right hand grasping the grating of the cage. When touched on the head it reacted weakly; when stroked it submitted readily and subsequently retired to the back of the cage. General sensibility, as well as taste and smell, appeared to be unimpaired. When a morsel of banana was thrown by the keeper, hitting the animal lightly on the body, it jumped slightly and, guided by the smell, picked up the morsel and ate it. There were rapid backward and forward movements of the left hind foot, at the rate of about 3 per second. At 1:30 p. m. the condition was unchanged, except that the upper and lower limbs on the left were paralyzed; the muscles on the left side of the face also appeared to be paralyzed, as the cheek on that side still contained food. On September 18, at 7:30 a. m., the monkey appeared to be in better condition. Paralysis of the left limbs had disappeared. Food was no longer retained in the left cheek. The animal was still blind. No further change was observed until 3 p. m., when there was a violent epileptic fit, from which the animal recovered but appeared to be exhausted. When it was seen at 5 and 7 p. m., there was obvious paralysis on the left side, and blindness continued. At 7:30 a. m. on September 19 the monkey appeared much weaker. There was frothing at the mouth. The left arm only was paralyzed. Blindness persisted, and the pupils were dilated (about twice as much as on the previous day). The animal slowly rotated about its own axis, always to the right. There were spasms of the muscles of the left eyebrow, with twitching of all the other muscles of the face, including rapid closing and opening of the eyelids. The animal remained in a corner, leaning against the wall at the back of the cage, with the head raised. A colorless liquid, resembling saliva, ran from the mouth. A noise made by passing a pencil through the grating or by hitting the floor of the cage caused no movement. When a door was banged violently, the animal raised its head and then dropped it. It lapsed into a state of deep coma. At 9 a. m. it had another fit, from which it had not recovered by 11:30 a. m. There was abundant salivation. The animal slept a few minutes before another attack. At 1:45 p. m. the condition was unchanged and at 2:35 p. m. a cinematographic record (fig. 1, *A* to *F*) was taken, followed by a detailed neurologic examination.

The animal lay on the right side, with the right front limb close to the body and the fingers flexed and twitching slightly. The mouth was open and filled with froth. The pupils were dilated, but reacted to light. During the fit, hyperextension of the spine, with extension of the forelimbs and flexion of the head on the chest, was noted. There were an oscillating movement of the eyeballs and twitching of the masseter muscles. Saliva was abundant during the attack. Afterward, the animal passed into a comatose condition, with the eyes closed, and for about ten seconds did not react to sensory stimuli. Gradually, twitching of the muscles of the right hand commenced again, and another fit occurred. In the early stages of the seizure the tendon reflexes were extremely active. There was ankle clonus on both sides. Plantar stimulation produced normal flexion. Toward the end of the attack the knee and ankle jerks were difficult to elicit. On plantar stimulation of the lateral aspect of the foot a typical triple response resulted in flexion of the four small toes and the large toe, flexion of the leg

at the hip joint and extension of the entire foot. This response was occasionally bilateral. Between the attacks the plantar response was normal, even on the affected side, and the triple response just described disappeared shortly after the attack.

Lumbar puncture was performed. The spinal fluid was clear, with 80 cells per cubic millimeter. Differential count revealed 41 lymphocytes, 11 polymorphonuclear cells and 28 mononuclears; the albumin content was 80 mg. per hundred cubic centimeters; colloidal benzoin reaction was 000012222210000; no bacteria were present. Examination of the blood revealed 46 per cent neutrophils,

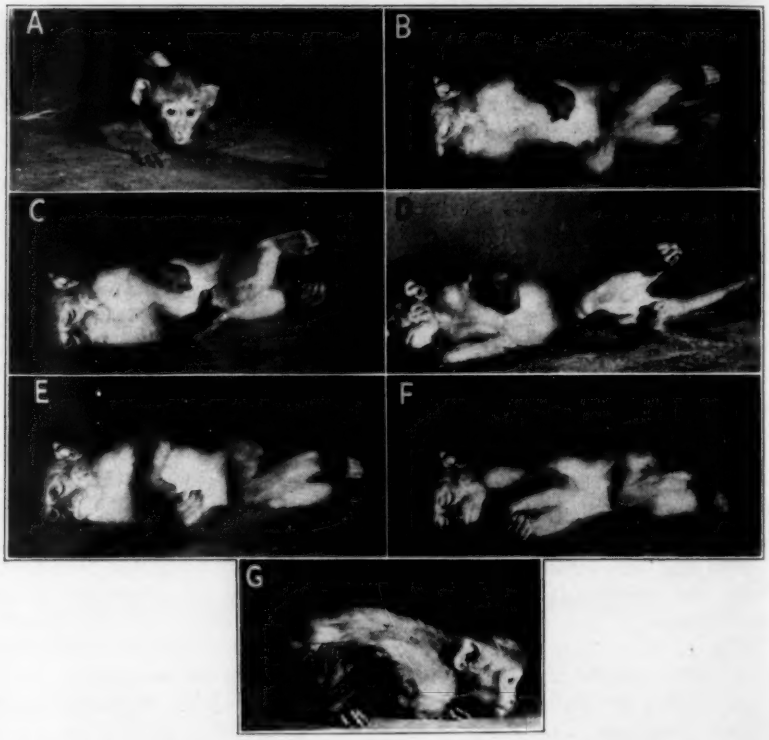

Fig. 1.—Cinematographic record (*A* to *F*) for a Macacus rhesus monkey (case 1). The animal is blind. *A*, slight paresis of the upper right limb. *B*, beginning of a jacksonian fit in which there are alternating movements of the upper right limb. Note the contraction of the muscles of the face and the orbicularis oculi muscles. *C*, diplopia and the tonic phase of the fit, involving the four limbs. Circumduction movements of the tail were marked. *D*, acme of the fit, with hyperextension of the neck and spine, forced pronation of the four limbs and circumduction movements of the tail. *E*, the close of the fit. The eyes are still open; the tail drops; the arms and legs are relaxing, and respiration is slow. *F*, deep postepileptic sleeping, with regular respiration. The eyes are closed. *G* (case 2), abnormal crawl position. The animal is blind, but hears and sniffs alternately. There is as yet no paralysis.

1.8 per cent eosinophils, 3.2 per cent transitional forms, 0.97 per cent monocytes and 30 per cent lymphocytes. The animal was killed September 19 at 7 a. m.

The clinical history was typical. The illness began with epilepsy, followed by psychic excitability, and was accompanied by blindness. Jacksonian fits occured, affecting the face and limbs, and were accompanied by opisthotonos and abundant salivation. In the postparoxysmal period, at a time when the tendon reflexes could not be elicited, we observed an excellent extensor plantar response with triple flexion: this response was occasionally bilateral. These phenomena disappeared as soon as the animal recovered from the comatose state. The illness ran a course of four days, during which there was an undoubted monocytic meningeal reaction of the cerebrospinal fluid.

CASE 2.—A male monkey (Macacus rhesus [India]), aged 2 years, had been at the zoo since January 1935. The food consisted of vegetables, fruit and rice.

On Aug. 22, 1935, it was observed that the animal had trouble in walking; there were ataxia and impairment in eyesight. It frequently struck its nose against the bars and wall as if it had not seen them. In the morning it had a fit of no great severity. On August 23 there was a succession of epileptic fits, each of short duration, starting with extension of the head and followed by twitching; at the same time the animal fell to the right. The pupils were dilated. These fits were followed by deep sleep. Some of the attacks were very short, with slow rotation of the head to the right, the whole body being drawn to the same side. The animal tried to draw itself erect, but collapsed and for several seconds had generalized twitching. On August 24 ataxia and hypermetria of the left arm and leg were observed (fig. 1 *G*). The animal jumped badly and excessively. The tendon reflexes were brisk on the right and weak on the left. The left knee jerk was absent. There was no response to plantar stimulation. Mydriasis was present, with preservation of the pupillary reflexes; yet the animal was totally blind. A hand passed before the eyes did not cause it to draw back. Nystagmus was not visible, although there was vertical oscillation of the eyeballs. The animal was in a state of collapse, preferring to lie on the stomach, asleep. It took food and apparently heard well. The general condition was poor. During the night of August 24 there were no fits. When examined on August 25, the animal had enough strength to take food from the hand, but ate little. The grasp of the right paw was weaker than that of the left. The pupils were dilated; the eyeballs tended to turn upward or to the side, reminiscent of the nystagmus of the blind. The animal moved about with caution. When jumping, it hurt itself against the partitions. The gait was hesitant, but there was no stumbling. From time to time the head drooped to the side, and there were violent twitching movements. The keeper told us that on the previous day there had been a period of ataxia of several hours. In the evening there was incomplete paralysis of the four limbs. The animal was able to move about slowly in the cage, tending to lift the extremities unusually high. It died on August 26.

In this case the illness lasted only four days. The onset was characterized by ataxia and impairment of vision and was followed by epileptic fits. Hypermetria of movements was pronounced, and the knee and ankle jerks disappeared early, without return. Two other monkeys were affected at the same time, but both recovered.

CASE 3.—A male monkey (Macacus rhesus), aged 2½ years, had been at the zoo since May 27, 1935. The customary food was taken.

On Sept. 28, 1935, at about 1 p. m., the animal was found in an epileptic fit. After it had received the customary treatment it was isolated. Like the other animals, it was very sleepy and appeared to be blind after the fit. No more attacks were observed on that day, and the animal recovered slowly. That night, at about 10 p. m., examination in strong electric light showed that the animal reacted slightly and was still blind. In the morning it was found to be normal. The monkey was transferred to the department of Prof. J. Rodhain for lumbar puncture and examination of the blood. Lumbar puncture revealed 51.7 cells per cubic millimeter, 59.2 per cent of which were lymphocytes, 33.3 per cent monocytes and large lymphocytes and 7.4 per cent polymorphonuclear cells. The colloidal benzoin reaction was 000112222210000. The albumin content was 70 mg. per hundred cubic centimeters. Vision became normal on the second day. The animal was observed for about a year, during which no more fits occurred.

The illness in this case lasted only twenty-four hours. One morning the animal had an epileptic fit and became blind, when it was isolated. On the same evening sight had not returned, but no further fits had occurred. On the following day the animal appeared normal. The lumbar fluid, twenty-four hours after the onset, showed a definite meningeal reaction, with excessive albumin. The animal was kept under observation for about a year, during which there was no recurrence of symptoms.

The symptoms and signs in this case were not as marked as those in the preceding cases, and the illness was of short duration. Spontaneous recovery took place in a few hours. The following case was similar, but we were unable to obtain a lumbar puncture.

CASE 4.—A female monkey (Macacus rhesus), aged 3 years, had been at the zoo since January 1935. The usual food was taken.

On Sept. 30, 1935, it was noticed that the animal staggered. When attempts to catch it were made, an epileptic fit occurred. The monkey was immediately placed under observation, and two other fits were seen; these were of short duration and were not severe. By midday sight appeared affected; the animal did not draw back when a hand was passed before the eyes. It was difficult to handle. There was hyperesthesia of the whole body, which made the animal resist energetically; when touched, it bit. Neurologic examination was not possible. At night the animal was again normal.

CASE 5.—A female monkey (Macacus rhesus), aged 20 months, had been at the zoo since May 1934. The usual food was taken.

On Oct. 6, 1935, in the morning, the monkey was found to be blind and unable to walk correctly. Because of blindness it was easily caught. Neurologic examination gave essentially normal results. Plantar stimulation caused flexion. No fits were observed. By noon on the next day the animal had recovered, and sight had returned to normal. There was no fever, the rectal temperature being 36.8 C. (101.5 F.).

The last animal of the 1935 series was killed ten hours after observation of the first symptoms, in an attempt to reproduce the disease by

inoculation of another animal with the brain substance and to determine whether nuclear inclusions were present.

CASE 6.—An adult male monkey (Macacus rhesus) had been at the zoo since May 21, 1935. The food consisted of fruit.

On the morning of October 8 the keeper, when feeding the monkey, noticed that it had become blind. Gait was hesitant, and the animal groped about. There was no ataxia, nor had the animal been observed to have a fit. Pupillary reflexes were present. During the morning there was marked dilatation of the pupils. In the afternoon there was no change, and no fits had been observed. The animal was killed by means of chloroform at 5 p. m.

The left occipital lobe and the right cornu ammonis were fixed in Zenker-Brazil solution and a small amount of alcohol, with a view to the study of possible nuclear inclusions. The right occipital lobe was ground up in physiologic solution of sodium chloride, and 0.25 cc. of this emulsion was injected intracerebrally into a healthy Macacus rhesus monkey and 2 mice.

During the days immediately following, the inoculated monkey showed no special symptoms. On December 30 it was found to be dying and was forthwith killed. Autopsy showed pulmonary and subcutaneous tuberculosis. Because of these lesions, Professor Rodhain did not make reinoculation. Examination of the brain revealed fairly abundant cerebrospinal fluid, which was collected and centrifuged. No tubercle bacilli were observed. The brain was placed in fixing fluid.

It will be seen that the symptoms in case 6 were similar to those in case 5. They were those associated with sudden amaurosis. The animal was killed as early as possible, in order to permit a study of the lesions at the onset of the disease, an attempt at transmission of the disease and an investigation of the cerebrospinal fluid.

Inoculations of ground brain substance by Professor Rodhain under experimental conditions gave negative results. The cerebrospinal fluid was normal, although typical cerebral lesions were seen, as will be described later.

During 1936 5 additional cases were observed, in only 1 of which was there a fatal outcome. The illness of the animals which recovered showed no particular features.

CASE 7.—A female monkey (Macacus rhesus), aged 1½ years, had been at the zoo since March 29, 1936. The food was fruit.

The animal was found blind in a large outdoor cage on July 3. It appeared to be exhausted and sleepy, defending itself only when touched. Hyperesthesia of the face was present. The animal was isolated on July 4. On examination on that day, the tendon reflexes were active, and plantar stimulation gave a flexor response. The abdomen was retracted. The pupils were dilated, and the animal was blind, though the right pupillary reflex was preserved. Movements were unsteady, with pronounced dysmetria of the lower limbs. On July 5 there was slight improvement; the animal was more lively, and sensibility seemed normal. It was no longer possible to make examination, owing to the liveliness of the animal. It was returned to the large cage. On July 11 it was found to be dying. The slightest touch caused it to groan. The reflexes were preserved. It was difficult to tell whether the animal was blind, as the eyes were closed. When the eyes were opened forcibly, it was impossible to attract the attention of the animal. On July 12 the condition was much as before. The animal seemed exhausted. No epileptic fits had been observed. It could no longer stand upright.

Lumbar puncture revealed that the fluid was clear and contained a fair number of erythrocytes (80 per cubic millimeter) and 61 leukocytes, 19 of which were polymorphonuclear cells. The albumin content was 5 mg. per hundred cubic centimeters. No bacteria were seen. On July 12 the animal was in the same condition as before, though much exhausted. No epileptic fits had occurred. On July 13 it was found dead in the cage.

The early stages of the illness in this case were typical and were followed in two days by temporary improvement, sufficient to permit return to the common cage. Six days later there was a relapse, and the animal died three days thereafter.

Comment.—1. Acute amaurotic epilepsy is a disease of the late summer and early autumn (table 1); it is characterized by sudden onset, unassociated with fever, and affects both sexes. The mortality is about 50 per cent. There are no neurologic sequelae.

2. When fully developed, the disease is accompanied by a slight meningeal reaction (table 2). There is an increase in the cell and the

TABLE 2.—*Observations on the Cerebrospinal Fluid of 5 Monkeys with Acute Amaurotic Epilepsy*

Case No.	Cells per Cu. Mm.	Polymorphonuclear Cells, %	Monocytes, %	Lymphocytes, %	Albumin, Mg. per 100 Cc.	Red Cells per Cu. Mm.	Colloidal Benzoin Reaction
1	80	11	28	41	80	63	000012222210000
3	51.7	7.4	33.3	59.2	70	..	000112222210000
6	9.6	4.2	2.1	4.3	..	472.5	.....
7	61.9	16	20	25.9	50	80	.....
9	10	2	2	6	40	20	000001222100000

albumin content of the cerebrospinal fluid, and the colloidal benzoin reaction is abnormal. Examination of the spinal fluid for cells showed 80 cells per cubic millimeter in case 1 and 51.7 cells in case 3. This is from five to ten times the normal figure described by Mollaret. The albumin content is from 70 to 80 mg., as compared with the normal content of from 20 to 30 mg. The benzoin reaction differs from that of animals used as controls. This meningeal reaction is not met in every case. In case 6, in which the animal did not have fits and was killed about twelve hours after the onset of symptoms, the spinal fluid was normal. Similarly, the spinal fluid in case 9 may be considered normal, though there was a slight increase in the albumin. Lumbar puncture was performed after the second epileptic fit, at the time of onset of the amaurosis; the animal recovered in three days. One may ask therefore if the absence of this meningeal reaction in the lumbar fluid indicates the absence of severe cerebral lesions.

3. The accompanying tabulation gives the results of examination of the blood of the animals observed in our series, as compared with those

of 4 animals used as controls. Dr. Verschraegen, head of the biologic laboratory, assisted in these examinations.

Case No.	Nonsegmented Neutrophils, %	Segmented Neutrophils, %	Lymhpocytes, %	Monocytes, %	Eosinophils, %
1	3.2	46	30	19	1.8
2	2.7	48	43	5.3	1
6	5.5	34	53	6	1.5
9	3	51	39	7	–
Control 2	1	43	52	4	0
Control 3	1	63	32	3	0
Control 4	1	45	51	1	1
Control 5	1	51	45	3	0

We found in the sick animals, therefore, a slight, but consistent, increase in the nonsegmented neutrophils and monocytes; these alterations were minimal, however, and it is difficult to draw from them any definite conclusions.

4. It was not possible to transmit the disease to an animal of the same species by intracerebral inoculation. Further, Professor Rodhain was unable to demonstrate the presence of cellular inclusions, such as Negri or Joest bodies. When our first paper was published, we did not know of any condition in human beings which resembled that which we described as occurring in monkeys. Recently, however, Jansen, Környey and Saethre [2] reported a case of a pathologic condition in a retarded child aged 14 who had peculiar epileptic attacks. The seizures were somewhat jacksonian, commencing first on the right side and then on the left. At other times the fits were generalized, resembling grand mal. Between the attacks were observed small contractions limited to one half of the body, which were followed by paresis. At an early stage astereognosis was noted, with ataxia of the extremities; several months after the first fit visual hallucinations were recorded. Later, there was progressive diminution of activity, leading to eventual blindness. Late in the development of the illness the patient became demented, dysarthric and incontinent; there was marked ataxia of the upper and lower extremities; the spinal fluid showed a moderate increase in globulin with pleocytosis. There were no signs of tuberculous meningitis.

Clinically, this interesting case, reported by Jansen, Környey and Saethre, in which there were jacksonian epileptic fits, terminating in amaurosis, is reminiscent of our cases in monkeys. We shall discuss the parallelism further in the description of the pathologic changes.

2. Jansen, J.; Környey, S., and Saethre, H.: Hirnbefunde bei einem Fall mit epileptiformen Anfällen und corticalen Herdsymptomen, Arch. f. Psychiat. **105**:21, 1936.

PATHOLOGIC OBSERVATIONS

METHODS

Frontal sections at all levels of the two hemispheres were examined histologically, and intermediate sections were studied when indicated. Sections of the brain and spinal cord were stained by the methods of Nissl, Spielmeyer, Cajal, Herxheimer and Achucárro. For the study of other organs, the usual hematoxylin and eosin stains were used.

DESCRIPTION OF CASES

CASE 1.—The meninges showed areas of polymorphonuclear infiltration (fig. 2) on the surface of both the occipital and the orbital region. The sulci were intact, but in them were occasional lymphocytes, with slight fibroblastic proliferation. These changes were strictly focal. The leukocytic infiltration did not appear to

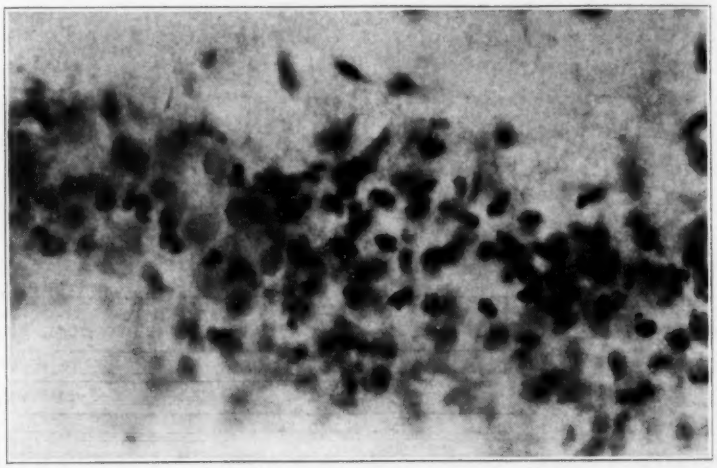

Fig. 2 (case 1).—Polymorphonuclear leukocytes in the pia mater. Nissl stain.

have a special predilection for the external part of the meninges (which we observed in certain of the cases studied in 1934). Frequently, infiltration of the internal layer of pia mater could be seen, without penetration of the cerebral tissue.

The greater portion of the molecular layer of the cortex showed pronounced macroglial proliferation (fig. 3). The macroglia cells were much more numerous than normal and had larger, clear nuclei, frequently with well developed nucleoli. With the Nissl stain the protoplasm was distinctly visible. *Gliarasen* were occasionally seen. The macroglial reaction was well marked at all levels, and it was always much more pronounced in the sulci than on the surface of the gyri. In the latter regions the macroglia was practically normal, though here and there slight microglial proliferation could be seen.

The other layers of the cortex showed slight macroglial and vascular proliferation. There was occasional slight proliferation of the endothelium of the capillaries, without any evidence of a parenchymatous lesion.

The parenchymatous lesions of the cortex were pronounced in the occipital and parieto-occipital regions. Their distribution was irregular, and they were seen only on careful inspection. In certain areas (e. g., the area striata) low power

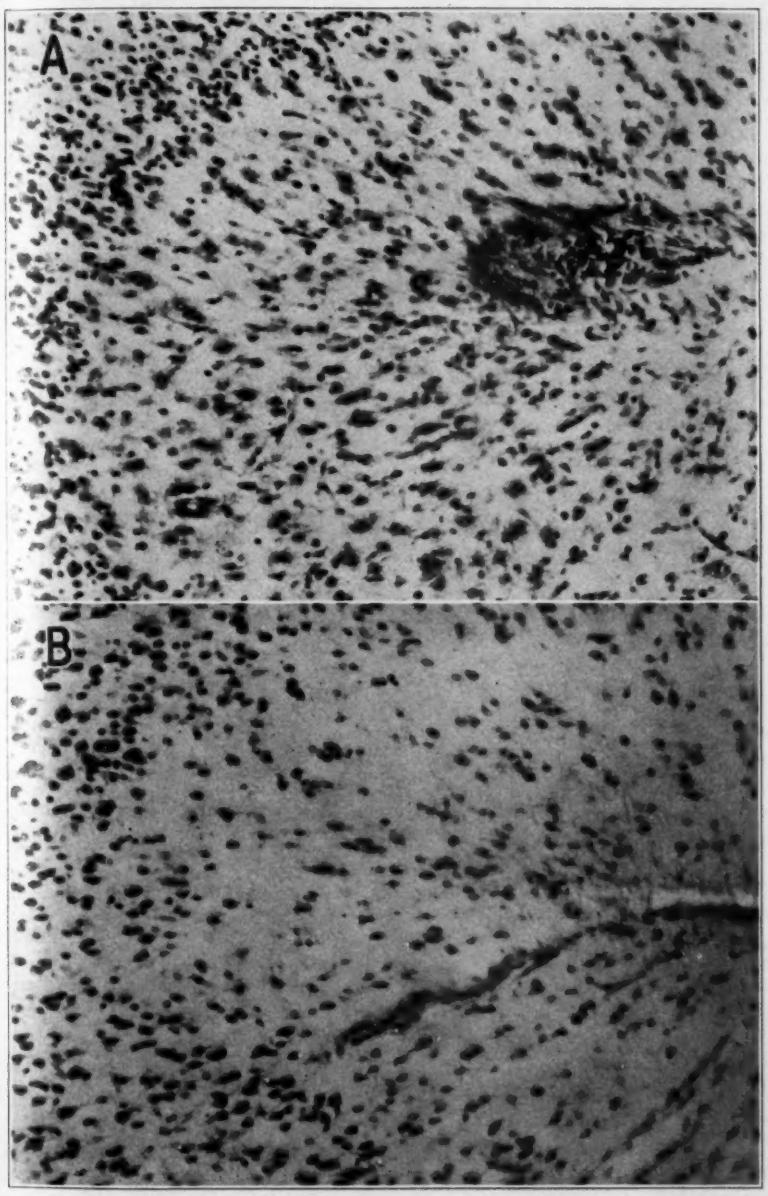

Fig. 3 (case 1).—*A*, marked macroglial proliferation in the molecular layer. The glia cells are more numerous; their nuclei are clearer and larger, and their protoplasm stains better than in the preparation (*B*) used as a control. Nissl stain.

magnification was sufficient to demonstrate them (fig. 4). Ribbon-like necrobiosis of the cortex (*Erbleichung*) was observed on both sides of the sulcus, the lower portion of which was intact. With a low power hand lens, one could discern without difficulty that layers II and VI were relatively well stained. Microscopically, the lesion was more pronounced in layers III to V. Here the Nissl stain was not absorbed, and the nerve cells had partly disappeared or showed marked degeneration (fig. 5). Cells with a shrunken, black nucleus, without definite structure of chromatin material and without nucleoli, were observed. The surrounding protoplasm was homogeneous and pale and lacked tigroid bodies; the cells were often triangular. In short, the picture was typical of the "ischemic cellular lesion" of Spielmeyer. Not infrequently, the morphologic pattern of the lesion approached the *schwere Zellerkrankung* of Nissl. In such cases either

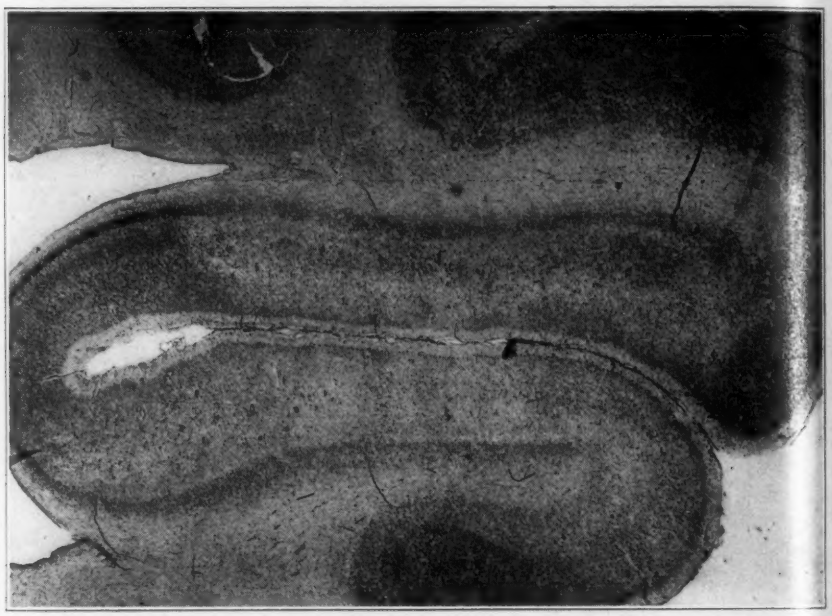

Fig. 4 (case 1).—Cortical laminar necrobiosis (*Erbleichung*) on both sides of a sulcus, the lower portion of which remains free. Cresyl violet.

the glia cells showed involutional changes or there was occasional evidence of commencing macroglial proliferation with numerous *Gitterzellen*. The scarlet red stain confirmed this and demonstrated the presence of neutral fats both in the fixed and in the mobile glia cells. The vascular proliferation in some places was marked, whereas in others it was lacking. In the involved areas the cortical myelinated fibers had entirely disappeared.

These changes were evidence of incomplete and recent necrobiosis of limited extent in the occipital region of both hemispheres and in the adjoining areas of the temporal and parietal lobes. In addition, in the insular cortex similar lesions of lesser severity were observed. The rest of the cortex did not show any clear evidence of parenchymatous involvement.

It was rare to observe perivascular polymorphonuclear infiltration in the cortex. When seen, it was usually in areas where vascular elements formed small nodules

(fig. 6 *B*) by local proliferation of the adventitia. It should be repeated that these nodules were rare and always small. There was no doubt as to their adventitial origin.

In the white matter, subcortical lesions, especially in the convolutions of the frontal, central and occipital lobes, were seen. These lesions were distinct in Nissl preparations, in which there was marked macroglial proliferation, with the glia nuclei frequently arranged in double rows parallel to the blood vessels. This we have shown previously. In the sections stained for myelin there was no evidence of demyelination at these levels, but with the scarlet red stain fatty material and some mobile elements were observed. These subcortical lesions were localized, but with ill defined margins.

Except for extensive and severe cellular lesions in both dentate nuclei, the basal ganglia, optic tracts, brain stem, pons, medulla oblongata and cerebellum showed

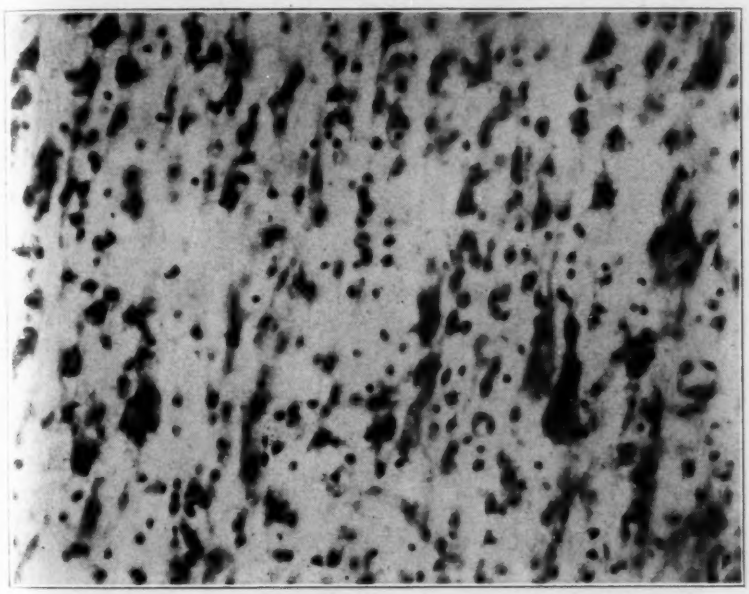

Fig. 5 (case 1).—Disappearance of nerve cells and ischemic cellular lesions, marked in the region of necrobiosis. There is no glia proliferation. Nissl stain.

neither focal nor diffuse lesions. No *Gliastrauchwerke* were noticeable in the cerebellum. The spinal cord and its meninges were intact. The internal organs showed no significant lesions, and there was no trace of tuberculosis.

Case 2.—Autopsy revealed signs of intracranial hypertension. The internal surface of the dura mater was tense and dry. The convolutions were flattened. The other organs showed no evidence of a pathologic state, except for congestion of the lungs. It is to be emphasized that there was no tuberculosis.

Microscopic examination revealed that the meninges showed no evidence of polymorphonuclear infiltration; occasionally collections of lymphocytes and macrophages were observed, and in the depth of the gyri there was a definite fibroblastic reaction.

The molecular layer showed well marked macroglial proliferation, though of a less pronounced character than that seen in case 1. Unlike the observation in case 1, there was no difference in the upper and the lower portion of the gyri, the infiltration being diffuse. In some places, immediately under the pia mater and within the molecular layer, typical *Gitterzellen* were seen (fig. 6 *A*). The deeper layers

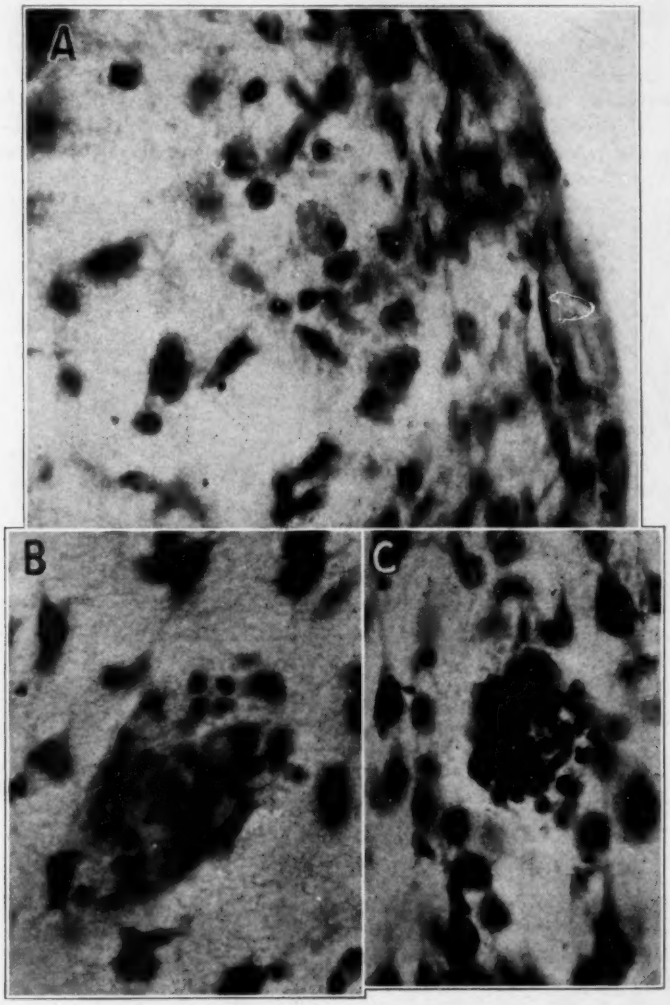

Fig. 6.—*A* (case 2), gitter cells in the molecular layer, just under the pia mater; *B* (case 1), intracortical vascular nodules with some polymorphonuclear cells in the cerebral tissue at that level, and *C* (case 2), vascular granuloma with polymorphonuclear cells, which are observed even in the cerebral tissue. Nissl stain.

of the cortex showed a diffuse, but discrete, macroglial and vascular reaction. This was especially pronounced in the temporo-occipital region. Here, some of the glia cells had the appearance of gemästete glia cells. In the cortex of this region we noted rare perivascular polymorphonuclear infiltration of the cortical tissue.

The parenchymatous lesions were slight and limited. In the occipital poles there was definite rarefaction of layers III and V, with pronounced vascular and macroglial proliferation, at times resembling gemästete glia cells. On the whole, the lesions in this case were much less pronounced than in case 1 and were limited to the occipital pole. The other parts of the occipital cortex showed only slight loss in nerve cells. Unlike the preceding case, well developed peri-

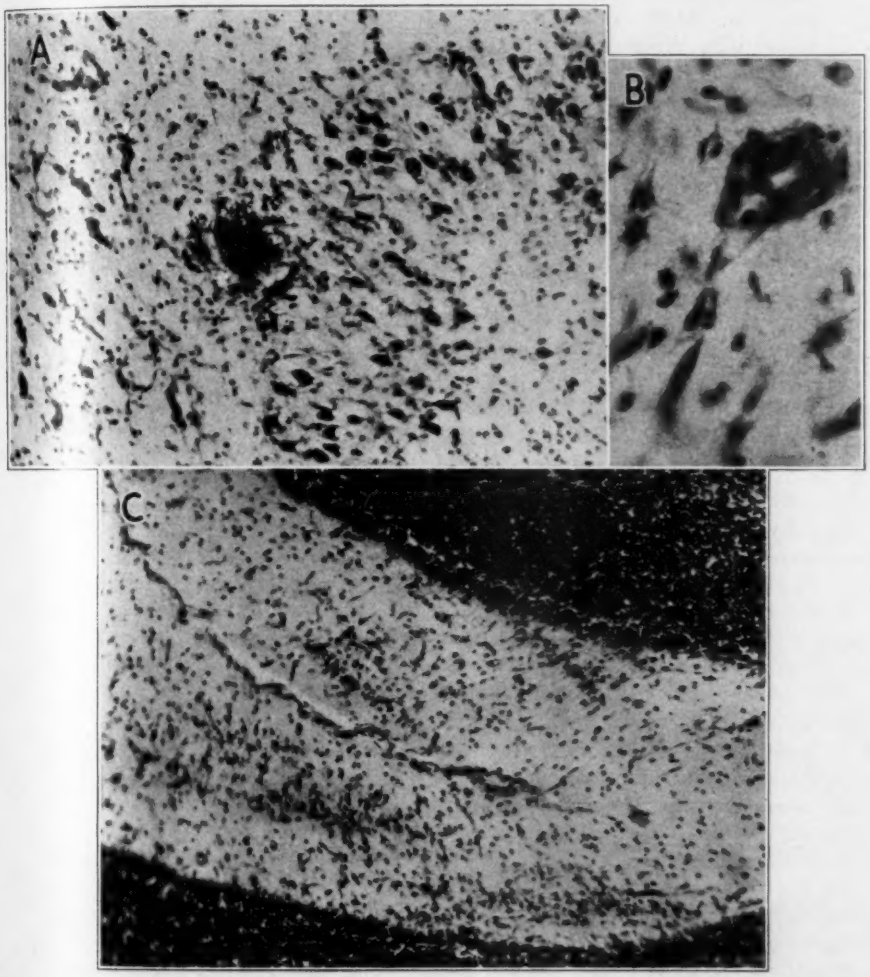

Fig. 7 (case 2).—*A*, granuloma in the olives, which is larger than that shown in 6 *C*; *B*, beginning of circumscribed nodular vascular proliferation, and *C*, typical *Gliastrauchwerke* in the cerebellar cortex. Nissl stain.

vascular nodules were seen frequently in all parts of the cortex (fig. 6 *C*), especially in the molecular layer. The nodules were also to be seen in other regions of the gray matter, for instance, in the olives (fig. 7 *A*). In the white matter they were rare. Though it was occasionally impossible to determine what elements

predominated in the larger nodules, one is led to believe, judging from the poorly developed nodules, that the reaction was adventitial rather than glial. In these small nodules there was circumscribed nodular proliferation of the vascular wall (fig. 7 *B*) without any glial proliferation.

Study of the cerebellar cortex revealed considerable loss of Purkinje cells and typical glial *Strauchwerke* (fig. 7 *C*), which was reminiscent of similar conditions in man. These glial structures were particularly numerous in the dorsal surface of the cerebellar hemispheres (lobus quadrangularis). The *Strauchwerke* always coincided with disappearance of the corresponding cells of Purkinje. When present, the Purkinje cells did not show any abnormality. The other layers of the cerebellar cortex were intact. The dentate nuclei showed no lesions, except for an occasional, but typical, area of neuronophagia and "syncytial" perivascular gliosis. The white matter of the cerebellum was intact.

The cerebral white matter, on the other hand, showed well pronounced parenchymatous lesions in the region of the occipital lobe (fig. 8 *A* and *B*). These were local, ribbon-like areas of demyelination, limited to the subcortical regions; the deeper parts were always intact. Sections stained with the Nissl method showed marked glial and vascular proliferation; the scarlet red stain revealed no evidence of fatty degeneration. In addition to the areas described, similar, though less pronounced, lesions were observed below the central cortex, but at no other levels. The basal ganglia, optic tracts, pons, cornu ammonis and brain stem were intact. The spinal cord, except for an occasional glial "star," was intact. Except for slight fatty degeneration in the liver, the other organs showed no microscopic lesions.

Case 6.—This case deserves special consideration because the animal was killed on the first day after the appearance of clinical symptoms. The meninges showed an occasional area of polymorphonuclear infiltration, of slight degree.

The diffuse gliosis of the molecular layer (superficial gliosis) was represented in this case by macroglial proliferation, which was not as pronounced as that in case 1. The gliosis was most marked in the occipital regions. *Gitterzellen* filled with neutral fat were seen just below the pia mater (fig. 9 *B*), but situated in the cerebral substance. At other levels there was also evidence of fatty degeneration limited to the superficial glia.

In all regions of the cortex one of the most striking changes was the extraordinary frequence of perivascular nodules. In figure 9 *A* is a typical example. All the layers of the cortex, including the subcortical white matter, showed this condition. The nodules varied in size, but most of them were large and dense. They were larger and more dense than those in case 2. More precise histologic study did not always reveal the cellular structure of these large nodules. In the less advanced stages the cells appeared to be purely mesenchymal and vascular. Figure 9 *C*, from a preparation obtained by the method of Cajal, demonstrates a typical nodule with definite vascular proliferation without any glial participation. In addition to the mesenchymovascular nodules, perivascular stellate nodules of purely glial origin were also seen; these nodules were more frequently observed in the brain stem (pons) than in the cortex.

Except for these nodules, the cerebral cortex showed no definite pathologic lesion. Macroglial and diffuse vascular proliferation was hardly noticeable; there was no loss of ganglion cells, even in the occipital region, nor was there any evidence of cellular degeneration. Nowhere was there leukocytic or lymphocytic infiltration.

The white matter, on the other hand, showed marked lesions, especially in the subcortical layers of the occipital lobe. These lesions were not easily studied in myelin preparations; Nissl preparations, however, revealed marked glial and vascular proliferation, with numerous glial "stars." Scarlet red stain showed in some places early evidence of fatty changes. The disintegration seemed to be in an active state, with little evidence of commencing mobilization. Similar sub-

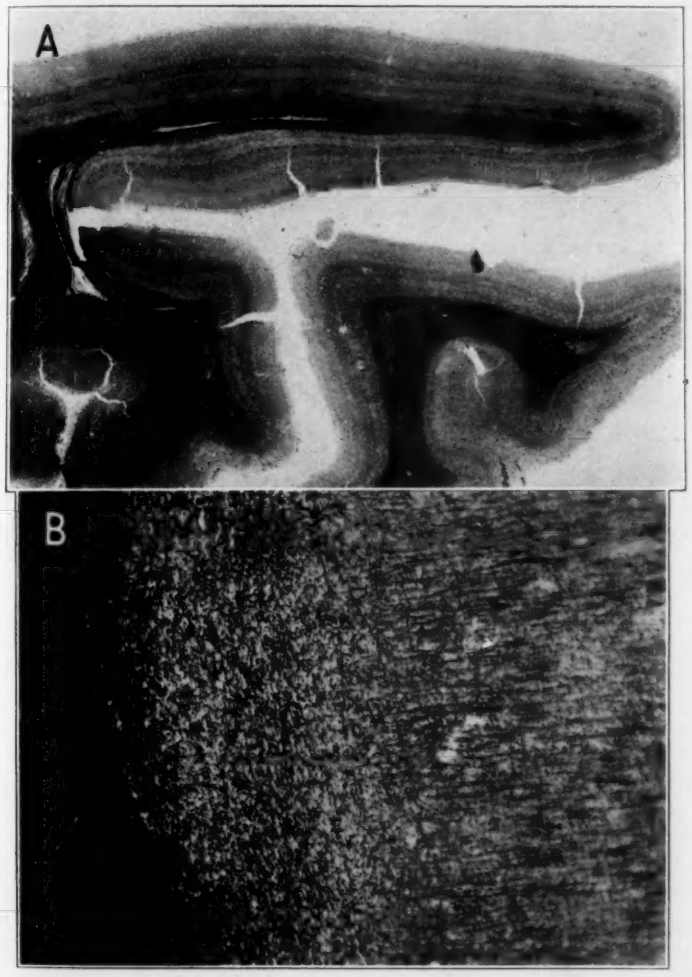

Fig. 8 (case 2).—*A*, focal and ribbon-like areas of demyelination in the occipital lobe, and *B* (higher magnification), aspect of partially demyelinated area under the occipital cortex. Spielmeyer stain.

cortical changes, though of a lesser degree, were seen in the central and frontal lobes.

The optic tracts, basal ganglia and brain stem were practically free from any definite involvement, except for a single glial *Strauchwerk* in the molecular layer

of the cerebellum. The dentate nuclei, the spinal cord and the spinal meninges showed no evidence of lesions. The other organs, namely, the kidneys, liver and myocardium, presented neither microscopic nor macroscopic lesions.

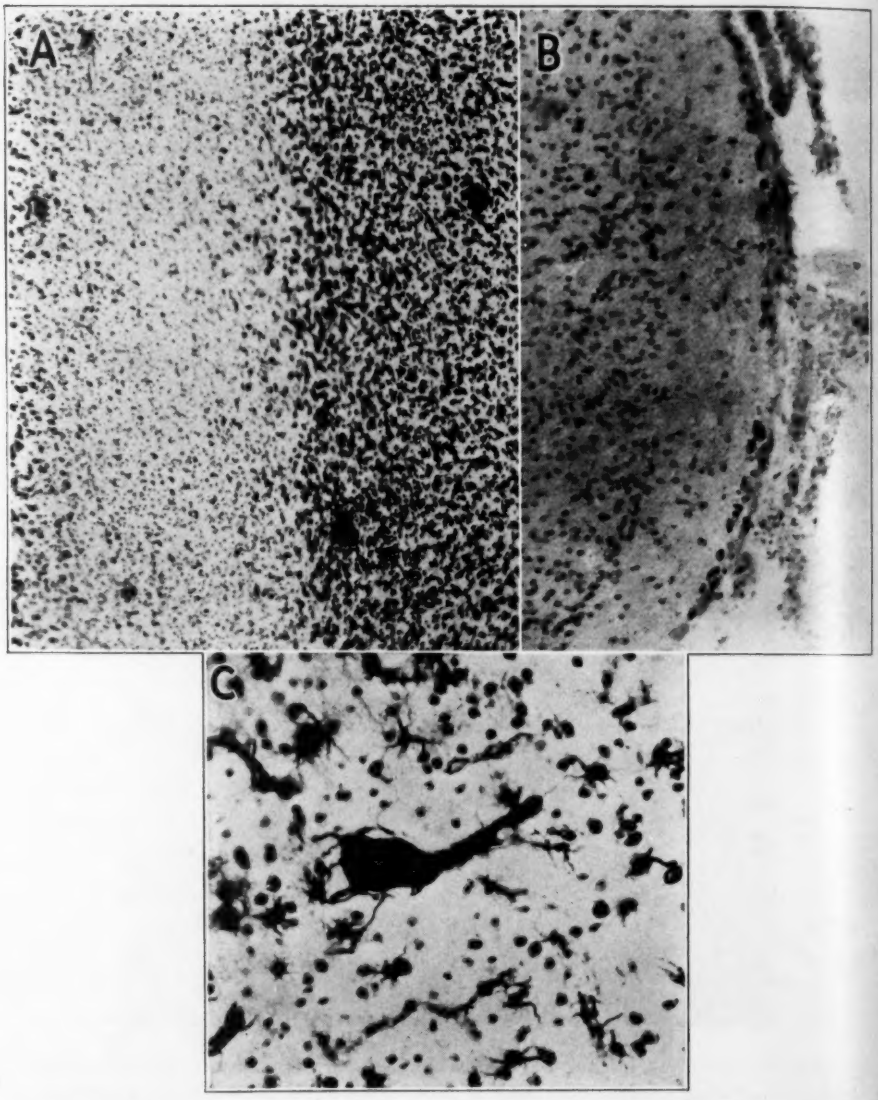

Fig. 9 (case 6).—*A*, small vascular granulomas; Nissl stain. *B*, granular bodies, loaded with neutral fats, in the molecular layer, just under the pia mater; scarlet red stain. *C*, lack of participation of glial cells in the formation of vascular nodules; Cajal stain.

CASE 7.—The meninges showed only slight involvement. Here and there were areas of fibroblastic proliferation. In the depth of one occipital sulcus lymphocytes, macrophages and isolated polymorphonuclear cells were observed.

The molecular layer showed diffuse macroglial proliferation, of moderate degree (fig. 10 *A*). The proliferation was more pronounced in the two occipital lobes, where it showed the same degree of intensity in the superficial as in the deeper portions of the gyri. What was characteristic in this case was the tendency of the macroglia cells to form a bandlike zone immediately under the pia mater. Figure 10 *B* shows such a band, the cells of which had a clear nucleus, wide protoplasmic halo and a tendency to the formation of *Gliarasen*.

The other layers of the cortex usually showed diffuse macroglial, but no vascular, proliferation. Here and there an "ischemic" cellular lesion was noted, with discrete loss of nerve cells. In the occipital region the lesions became more pronounced, with greater loss of nerve cells. Usually this loss was discrete, though definite, especially in layers III, IV and V, as shown in figure 11 *A*. As may be seen, the lesions were limited to certain layers and were extensive in both occipital lobes. They involved both the convex and the concave surface, without any predilection for the visual area. In some places, as demonstrated in figure 12, the loss of cells was massive, without actually attaining the degree of *Erbleichung*.

In the same illustration there can be seen marked proliferation of protoplasmic macroglia cells, with numerous gemästete forms, and pronounced vascular proliferation. The subcortical white matter of the occipital region showed the same glial proliferation without the presence of neutral fats. There were marked symmetric lesions in the subcortical white matter and the adjoining cortex at two other levels—in the central region of the cortex and in a few of the orbital convolutions. Here there was marked macroglial reaction with numerous gemästete glia cells; no demyelination had taken place. These foci of degeneration were not circumscribed, but extended into the deeper layers of the cortex. Thus, one saw in layers VI and V the same degree of marked macroglial proliferation as in other regions, with definite loss of ganglion cells in some places and the presence of numerous nerve cells in others, corresponding to the description of "ischemic" and "severe" cellular lesions.

The cornu ammonis on one side showed a typical vascular lesion of Sommer's sector. Throughout the greater extent of this sector the nerve cells had partially disappeared; the remaining cells showed a "severe" type of cellular lesion. The molecular layer of the cerebellar vermis showed some glial *Strauchwerke*. In the dentate nuclei there were also some syncytial glial proliferation and loss in cellular elements. These changes were not marked.

The optic tracts, basal ganglia, pons, bulb and spinal cord showed no lesions.

It is to be emphasized that in this case, unlike the others, a glial vascular nodule was nowhere observed.

Comment.—In our former study, which included 3 pathologic observations, it was possible to state that the disease had definite anatomicopathologic character. Though there were important differences in the observations in each case, there were important points common to all sufficient to justify our impression. There was constancy in the localization of the lesions in the occipital region and, to a lesser degree, in the central region. The degenerative lesions were always essentially vascular. There was a constant diffuse macroglial and vascular reaction,

with perivascular nodules. The differences noted were essentially those of the degree and incidence of the inflammatory process. We expressed the belief that these differences probably represented various stages of

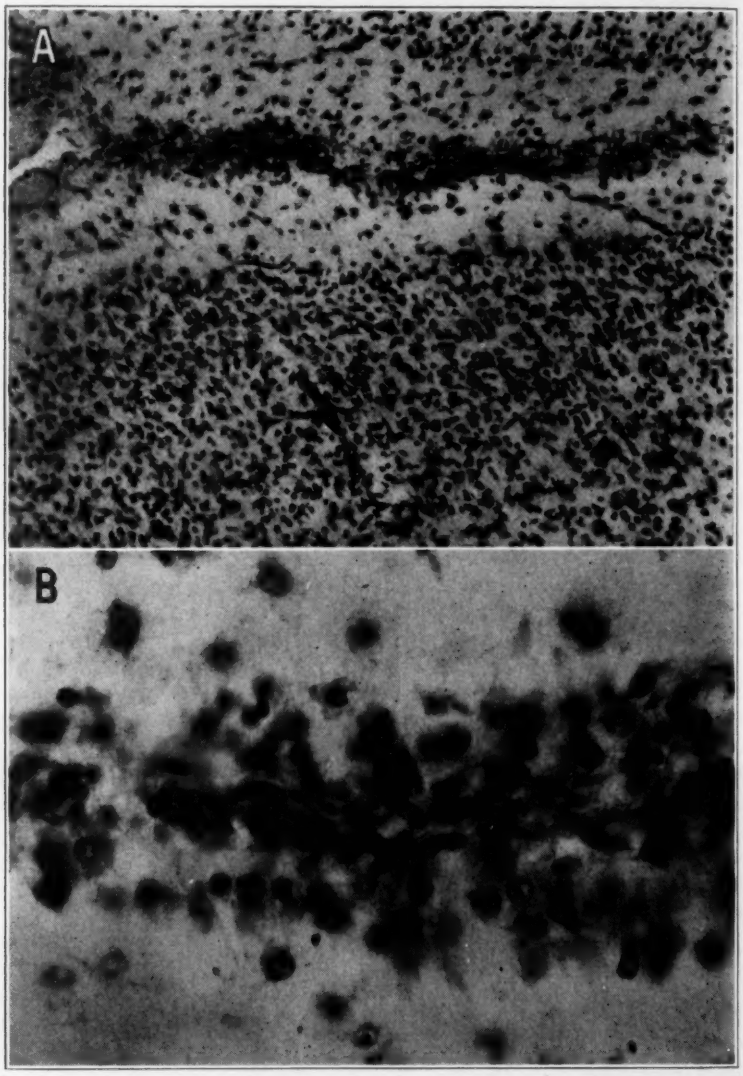

Fig. 10 (case 7).—*A*, diffuse capillary and macroglial reaction in the molecular and the deeper layers of the cortex, and *B*, macroglial proliferation forming a band at the surface. Nissl stain.

the same process. In order to present our observations graphically, we have tabulated those made both in the 4 new cases and in the 3 old cases (table 3). Too much stress cannot be placed on the importance of tabulation of such material.

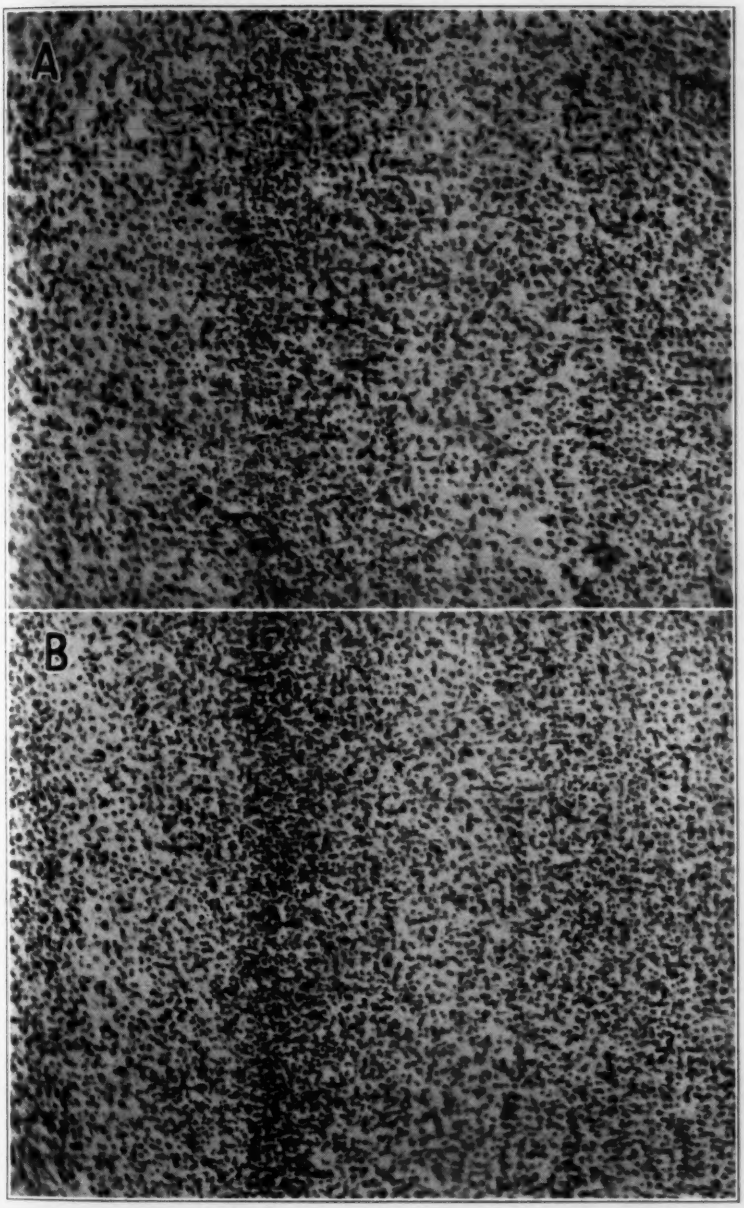

Fig. 11 (case 7).—*A*, discrete and diffuse loss of nerve cells and glial proliferation in layers III and V, as compared with a section (*B*) from a normal brain used as a control. Nissl stain.

On examination of table 3, it will be observed that in the 7 cases the following features appear in common: There is diffuse macroglial proliferation in the molecular layer. Early degenerative vascular lesions appear in the subcortical white matter, especially in the occipital region and almost always in the central area. The occipital and central cortex, except in case 6, showed analogous vascular involvement. In all the cases, except case 7, there were perivascular nodules. In every case there was involvement of the meninges, though occasionally of minimal degree.

The diffuse vascular proliferation and intracerebellar inflammatory infiltration were not constant in every case. It is to be added that the

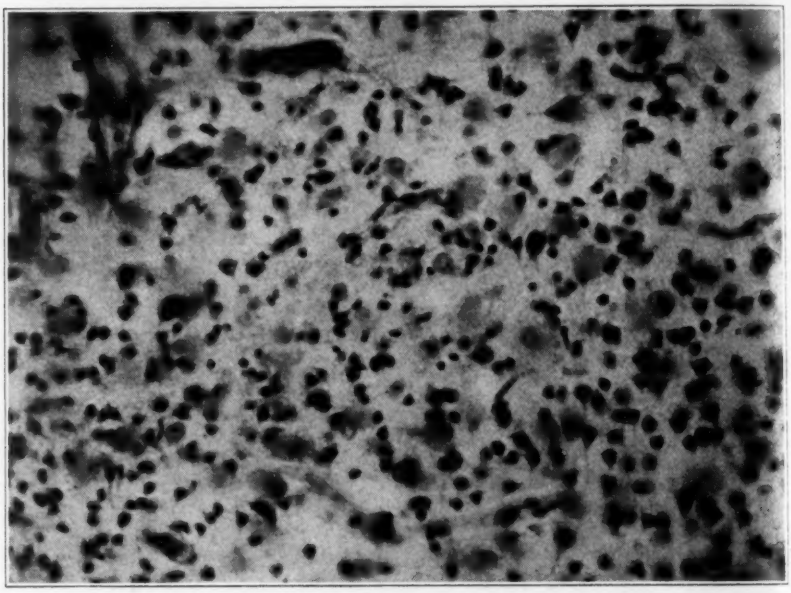

Fig. 12 (case 7).—Massive loss of nerve cells in the occipital cortex and marked reaction of the macroglia (gemästete) cells. Nissl stain.

cortical lesions always presented a vascular aspect, not only because of their laminated or pseudolaminated distribution but because of the "ischemic" character of the cellular reaction, the disappearance of the *Nisslgrau* and the character of the vascular and glial reactions.

In 1 (case 6) of the 2 cases which differed from the others, parenchymatous degeneration of the occipital cortex, the point which we consider as characteristic of the disease, was not shown. The animal, however, was killed at the commencement of the earliest clinical sign of the disease. It is to be noted that in all other respects the usual features were presented in this case and that there were typical lesions

in the white substance of the subcortical area of the lobes. Therefore we feel justified in considering this case as indubitably one of acute amaurotic epilepsy. Later, we shall insist on the importance of the absence of cortical lesions in the early stage of this disease. The other case (case 7) in which the picture was atypical is of importance because of the absence of perivascular nodules. Except for this absence, the pathologic picture agreed so well in all essential points with that in the other cases that we do not feel justified in considering another diagnosis. The absence of this vascular reaction, which possibly is of short duration, may be explained by the slow development of the disease (during a period of ten days) in this case.

TABLE 3.—*Pathologic Observations in 7 Cases of Acute Amaurotic Epilepsy Occurring in Macacus Rhesus*

Case No.	Duration of Disease, Days	Meningeal Infiltration	Intracerebral Inflammatory Infiltration	Perivascular Nodules	Degenerative Lesions: Cortex	Degenerative Lesions: Subcortical White Matter	Diffuse Vascular Proliferation	Diffuse Glial Proliferation: Layer I	Diffuse Glial Proliferation: Layer II-VI
Old series									
1	8	+++	++	++	+++	++	+	+++	++
2	3½; killed	±	—	+	+++	+++	—	++	±
3	3	++	++	+++	+	+	++	+++	++
New series									
1	4; killed	++	+	±	+++	++	+	+++	+
2	4	±	±	++	+	+++	+ Occipital	+	+
6	1; killed	+; in one place	—	+++	—	+++	—	++	±
7	10	±	—	—	++	++	+ Occipital	++	++

In attempting to explain the variability of certain reactions by the length of time after the onset at which death occurred, we are on difficult ground. This is especially so since the clinical manifestations of the disease are not always synchronous with the earliest evidence of pathologic involvement. This was demonstrated in case 6, in which there were already massive lesions though the animal was killed on the appearance of the first symptoms. We therefore advance our arguments briefly and with reserve.

The discrepancies between the clinical and the pathologic condition may be explained by the difficulties under which clinical observations are made. In spite of every care and attention, blindness or ataxic movements—even the first epileptic fit—may pass unperceived in a troop of 200 monkeys. This explanation, however, is not the only one, as animals 6 and 9 showed but little alteration in the spinal fluid. This absence of reaction in the spinal fluid must be closely associated with

the extreme paucity of the polymorphonuclear infiltration and the scarcity of perivascular nodules observed post mortem. Because of this, it is with prudence that we undertake a discussion of the correlation between the clinical and the pathologic observations in the various stages of the disease process.

The infiltration of the meninges is occasionally definite and purely leukocytic in character; in other cases, nothing but macrophages, lymphocytes and fibroblasts evidence the meningeal reaction. The infiltration is never diffuse, but always focal. It seems to be more pronounced in cases in which the disease is of long duration, though this is by no means the rule. It is only in cases in which there is a marked leukocytic meningitis that leukocytes are to be seen in the interior of the cortex. It is difficult to refer to the condition as "meningitis" or "encephalitis" because the lesions are too discrete and circumscribed.

The superficial macroglial proliferation is one of the most characteristic reactions, though the degree and extent are variable. It is unlikely that it is a consequence of meningeal infiltration, since the latter is always focal and the glial proliferation is always diffuse. It is difficult to relate these differences in degree with the clinical duration of the disease.

One of the most striking features is the great number of vascular or perivascular nodules in most cases. In our former study, we compared the appearance of such nodules with those associated with typhus. The resemblance is very close when the sections are studied under low magnification. However, it is not possible to hold the view of a similarity in origin of the two types since the mesenchymatous character of the nodules has been shown. The nodules in typhus are, according to Spielmeyer,[3] essentially of glial nature. It must be observed, however, that Spielmeyer admitted the possibility that some nodules contain vascular elements. The histologic difference between our nodules and those occurring in typhus may be explained as one of degree rather than of origin.

COMMENT

This disease demonstrates a complexity of lesions recognizable as sequels of circulatory trouble: meningeal (sometimes cortical) inflammatory focal lesions, diffuse macroglial and endothelial proliferations, discrete parenchymatous lesions and, finally, small vascular granulomatous nodules.

In our former work, it was not possible to offer an explanation of the cause of this neuropathologic picture—which was reminiscent of a generalized septic embolic process. This possibility, however, was elim-

3. Spielmeyer, W.: Die zentralen Veränderungen beim Fleckfieber und ihre Bedeutung für die Histopathologie der Hirnrinde, Ztschr. f. d. ges. Neurol. u. Psychiat. **47**:1, 1919.

inated at autopsy. In this paper, no further contribution as to the cause is possible. Moreover, the very symmetry and regularity of the sites of lesions of the vascular type cannot be explained on the basis of multiple emboli. We have also considered the possibility of a "functional" circulatory disturbance, such as may occur in association with human epilepsy. Indeed, we observed in our new series lesions similar to those in cases of human epilepsy (*Strauchwerke* of the cerebellar cortex and lesions of the cornu ammonis). Such lesions we did not observe in our previous study. It is indeed probable that these lesions are the result of the epileptic attacks, but one cannot explain so easily the extensive and singularly symmetric necrobiosis in the occipital cortex, subcortical white matter and other sites. It is even more difficult to explain the causes of the other changes.

In looking for comparable pathologic pictures, one is struck by the resemblance that this condition bears to certain intoxications. Mention was made in our earlier paper of the intoxications produced by Meyer and Blume [4] with carbon monoxide, cyanamide and various narcotics. To these we may add the observations by Adelheim, Amsler, Nicolajev and Rentz [5] on "toxic experimental encephalitis" produced by cicutoxin. In the work of Meyer and Blume, there was absence of inflammatory lesions, but Adelheim, Amsler, Nicolajev and Rentz showed that meningitis and true encephalitis may be produced by intoxication; further, Stief and Tokay [6] obtained with insulin a picture of cortical necrobiosis with marked inflammatory reaction in the meninges, and even locally in the cerebral tissue. These observations closely resemble those made on our animals. However, when taken in detail, differences are to be observed. We insist on this comparison with the lesions associated with the intoxications in question in order to point out that the histopathologic picture in our cases may result as much from an intoxication as from an infectious process. As our experimental work up to the present has not produced direct information as to the cause of the condition, the pathologic picture must not color future work on this problem. From a pathologic point of view, an infectious process as well as an intoxication must be considered as the hypothetic cause of this strange condition. Clinically, the severity of the disease, the absence of fever and the few alterations or even absence of abnormality, in the blood picture are

4. Meyer, A., and Blume, W.: Folgeerscheinungen der Narkose am Zentralnervensystem. Histopathologischer Teil, Ztschr. f. d. ges. Neurol. u. Psychiat. **149**:678, 1934.

5. Adelheim, R.; Amsler, C.; Nicolajev, V., and Rentz, E.: Experimentelle toxische Encephalitis durch Cicutoxin, Arch. f. Psychiat. **102**:439, 1934.

6. Stief, A., and Tokay, L.: Weitere experimentelle Untersuchungen über die cerebrale Wirkung des Insulins, Ztschr. f. d. ges. Neurol. u. Psychiat. **153**:561, 1935.

points in favor of a toxic process. Moreover, if the animal survives there are no sequelae. Autopsy on the animals attacked in 1934 which died in 1935 or 1936 of some other condition showed the absence of any residual cerebral lesions. This absence of residual lesions may also be invoked in favor of the possibility that the lesions are of vascular origin, the early lesions causing no permanent change but the more extensive lesions leaving parenchymatous changes.

As we pointed out in our first communication, the question of differential diagnosis does not arise, as no other nervous disease in the monkey need be considered for the simple reason that up to now no other syndrome in monkeys is known that in any way resembles that described in this paper. An exception must be made of a condition described by Bodechtel,[7] which bore only slight resemblance to that occurring in our animals. Only one other cerebrospinal disease in the monkey has been clearly defined from a pathologic description, namely, the syndrome which one of us (H. J. S.) [8] described as funicular myelosis with involvement of the white cerebral matter and the peripheral visual pathways. As this disease is limited exclusively to the white matter and its evolution is slow, confusion with acute amaurotic epilepsy is unlikely.

Since our former publication, only 1 case occurring in man has been reported—that by Jansen, Környey and Saethre. In this case the pathologic picture was similar to that in our monkeys. The authors of this report pointed out that the absence in their case of inflammatory reactions and the presence of vascular lesions in the cerebellum and the cornu ammonis was indicative of a different causal agent. However, we have observed in our new series of monkeys similar lesions in the cerebellum, but the absence of inflammatory phenomena and vascular nodules in the case reported by Jansen, Környey and Saethre represents a striking difference. It must not be forgotten, however, that in the case in man there was a chronic evolutionary process, which may explain the disparity in the pathologic picture. Once more, we are led to the question of the phases of the process. A study of the sequence of events permits the following conclusions.

The degenerative parenchymatous lesions, especially in the cortex, may still be absent when the vascular lesions, meningeal infiltration and glial proliferation are already well developed (case 6). The degree of cortical damage appears more pronounced in cases in which the evolution of the disease is somewhat longer than in those in which the animal

7. Bodechtel, G.: Spontanencephalitis bei einem Affen, Ztschr. f. Hyg. u. Infektionskr. **111**:331, 1930.

8. Scherer, H. J.: Funikuläre Spinalerkrankung mit schwerer Beteiligung des Grosshirnmarkes und Opticusveränderungen bei fünf Pavianen, Ztschr. f. d. ges. Neurol. u. Psychiat. **141**:212, 1932.

dies or is killed at the clinical commencement of the disease. The initial clinical phenomena (blindness and epilepsy) can, moreover, be explained satisfactorily on the basis of a functional vascular disturbance, and their total regression may thus be accounted for. Among these initial phenomena are transient palsies (case 1), which may later become more marked. In this way, it is possible to associate the grave parenchymatous lesions with the more marked and permanent palsies. The anatomic facts are in accordance with such an interpretation. The toxic or toxi-infectious origin of the two series of disorders remains to be discovered. It is our opinion that the cause must be sought outside the nervous system.

SUMMARY

We report a new series of observations on the nervous disease appearing in Macacus rhesus which we described previously under the name "acute amaurotic epilepsy." This study is now founded on 16 clinical and 7 pathologic observations. From a clinical point of view, the disease is characterized by blindness of central origin, epileptic fits, disturbance of movement and gait and a marked reaction in the spinal fluid. The disease may cause death or end in complete recovery. The evolution is always acute. During three years the disease has made its appearance in summer and at the beginning of autumn and has always attacked a small group of animals.

Pathologic examination shows a primary cerebral disease occurring in animals which are otherwise healthy; no septic embolic process is observed at autopsy. In the brain, parenchymatous lesions of the vascular type (recent necrobiosis) are seen in the cortex and in the subcortical white matter; these lesions are generally symmetric and localized chiefly in layers in the occipital lobes; they may occur in the subcortical, occipital and central regions. The following characteristics are also observed: marked diffuse macroglial proliferation in the molecular layer, a tendency to vascular and macroglial proliferation in the deeper layers of the cortex, circumscribed vascular nodules and a focal leukocytic meningeal reaction. In 3 cases *Gliastrauchwerke* were observed in the molecular layer of the cerebellum, similar to those seen in cases of human epilepsy. The peripheral visual paths, spinal cord and peripheral nerves are normal. The cause of the disease remains unknown. An infection as well as an intoxication is possible.

Case Reports

NEGATION OR REVERSAL OF LEGAL TESTIMONY

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The spontaneous, sincere and apparently completely unmotivated negation, reversal or alteration of condemnatory legal testimony previously given by credible witnesses constitutes a difficult and confusing problem. Although found more often by the psychiatrist than by the jurist, such change of testimony can, and not infrequently does, entail serious legal difficulties.

Such alteration of testimony is characterized by a complete change in the beliefs and understandings of the witness, effected by unrecognized factors within the personality. It occurs most frequently among the witnesses who are themselves the injured parties and, hence, have presumably every reason for telling only the truth, and it develops usually in relation to crimes of a personally horrifying, traumatic or repugnant character.

Because of the significance of this type of behavior psychiatrically as well as legally, the following material from the histories in two illustrative cases is presented as a clinical note for the purpose of directing attention to this phenomenon and to the need for an extensive analytic study of the psychologic mechanisms and processes involved in these occurrences. Such an analytic study is not proposed in this report, since the data available are limited largely to the original situation and the final outcome. Hence, an effort will be made only to indicate briefly the various psychologic factors and the psychic dynamisms contributing to the course of the developments.

The two case histories to be cited have been selected from among others because of the fully established facts of the original crimes, the detailed, factual and fully corroborated testimony elicited initially and the absence of external motivation in the eventual development of significant and completely contradictory attitudes and beliefs.

REPORT OF CASE

CASE 1.—This report centers around a police raid on a bawdy-house. Arrests were made of two girl inmates aged 9 and 11 years, their parents, who were the proprietors, and twelve male patrons. Full confessions were obtained individually from all the prisoners, those of the adults corroborating fully the essentially identical accounts given by the two girls. In addition, medical examination of the girls disclosed numerous bruises and injuries, substantiating their account of beatings, and also revealed that they had been subjected to vaginal and rectal coitus and infected with syphilis and gonorrhea, both rectal and vaginal.

From the Eloise Hospital.

In the legal disposition of the case, the two children were committed immediately to a custodial institution, where they were separated from each other according to the age grouping within the institution and kept for three months in "quarantine isolation" for treatment for the venereal infections.

At the suggestion of a colleague of wide experience in criminology who anticipated the eventual outcome, the two girls were interviewed separately, and an extensive account of the entire experience was obtained during the first week of their institutionalization, with three subsequent interviews thereafter, at intervals of two months. The girls' stories were found to be essentially identical and to agree in full with the accounts obtained later from the adult offenders, as well as with the original court testimony.

During the first interview, both girls were intensely desirous of securing a sympathetic listener, and both told the story readily, easily and completely, manifesting much unhappiness over and repugnance to their experiences. Also, they manifested intense fear and anxiety over their physical condition, as well as strong specific resentments and hatreds toward their violators and a sense of great satisfaction over the punishments accorded the adults. At the same time, it was noted that both girls recalled certain of their experiences with definitely pleasurable, though guilty, feelings and that they were quite shamefaced about their own active participation in certain aspects of their experiences.

A marked change in both girls was noted during the second interview. There was no longer a driving need to tell the story; emphasis was placed on the venereal infection, with the complaints centering around the inconveniences and the annoyance occasioned by the quarantine and therapy, and little mention was made of their former fears of what the disease would do to them. Many details of the original accounts were omitted; others were surprisingly vague or minimized. There was a general tendency to contradict and to deny previous statements. Close questioning on a few items disclosed definite reluctance, and even difficulty, in admitting certain facts, and the repugnance previously noted had been transformed into new resentments, especially in connection with the rectal coition. The resentments and hatreds noted previously were markedly increased by the addition of resentments concerning their immediate situation.

At the time of the third interview they had made good recovery from the gonorrheal infection and were much better adjusted to the institution. Although willing and ready to talk, they seemed to be interested only in immediate matters. Questioning about their past experience elicited an utterly inadequate account, in which even major details were denied or greatly minimized. Rectal coitus was emphatically and resentfully denied by both. There were flat denials of ever having been nude or of having danced exhibitionistically, and they had forgotten the names of half the men. There were many vague statements of "Ma didn't like those things" and "Ma wouldn't let anybody do those things." A few similar statements were made concerning the father. There was a tendency to declare certain of the more offensive details to be "lies" told by one of the men who had been particularly brutal. Furthermore, their reluctance or difficulty in giving any details of their story seemed to be greatly increased. Their affective reaction seemed to be one entirely of distaste and repugnance to the whole experience, and there was no evidence of pleasurable recollections; rather, there seemed to be an element of sadness and grief. Even the question of therapy for the venereal infections was casually glossed over as a routine health measure peculiar to their present situation, and all the earlier anxiety centering around their physical condition had disappeared. Likewise, the hate reactions centering around the original

experience now seemed to be limited to mild resentment over their own imprisonment. The former sense of satisfaction over the legal punishment of the adults had disappeared except for a feeling of pleasure that the man they now accused of lying was serving time.

The final interview was conducted six months after the first. A complete change in attitude was apparent in both girls, though more marked in the younger. Strong resentment was expressed over my interest in the story, and no information was given spontaneously except the emphatic inclusive declaration that it was "all a lot of nasty lies." A warm defense was given of both parents. The authorities were harshly criticized as unwelcome intruders into a private home, and the whole experience was minimized into the statement that "some bad men came to the house, but nothing bad happened." This statement was persisted in with such obvious sincerity and belief that resort was had to sympathetic questioning concerning the "lies" that had been told. After their confidence had been won with some difficulty, both recounted their original story in fair detail but branded each item as a "regular lie" told by various of the men while in court. Furthermore, they insisted sincerely that they had consistently told me the entire story as a "bunch of lies" maliciously concocted by some men who had had their parents arrested and imprisoned for illegal traffic in liquor. Even close questioning about the injuries sustained and the venereal infection elicited either resentful denials or trivial explanations, and they seemed to have no real recollection of the whole experience as an actual happening in their own lives. At no time could their sincerity or their full belief in their statements be doubted.

Case 2.—This report concerns a young man on parole from a penal institution. After stealing an automobile, he took a young woman for a drive, their intention being to spend the night at a road-house of ill repute. He did not disclose to her the immediate circumstances, although she was aware of his criminal history and legal status. During the course of the drive, as a result of recklessness, the car overturned, pinning the young woman beneath it, and burst into flames. The man freed himself but made no effort to rescue his companion, instead fleeing from the scene. Passing motorists rescued the girl, but not until she had been severely burned, in addition to receiving other serious injuries in the accident. The man was apprehended, and at the trial the girl, with much bitterness and hatred, and the motorists testified fully as to the facts, the truth of which the man confessed. About eight months later, without there having been intercession of any sort, the girl endeavored to secure a retrial of the case on the grounds that she had given false and mistaken testimony. The man, when interviewed by me, declared, "She's nuts! She told the truth the first time," and explained further that the relatively short sentence he had received did not warrant his undergoing the anxiety of a retrial, since his indisputable guilt in certain aspects of the case might result in a longer sentence.

The girl, when interviewed by me, was obviously sincere and believed fully that the man had exerted every effort possible to rescue her, giving full details of his endeavors by a process of retrospective falsification and misconstruction. She explained that her intense suffering and the long months of confinement during her hospitalization had made her realize how false her original account had been, since "no human being would do such a thing nor could anybody endure being so treated." She elaborated in detail on how one would feel if deserted, as she was said to have been, and declared that such an experience would be utterly "intolerable" and that one "could only imagine it but could

not possibly endure it." When confronted by each item of her original testimony, she misconstrued it so logically and exculpated herself for her "misstatements" and "intentional malice" so contritely on the grounds of the shock and pain she had suffered that she was most convincing, although psychiatrically the inferences to be drawn were quite otherwise. Even the prisoner's direct admission of the truth of her original account was casually disregarded. She insisted rather compulsively that something be done to prove legally that the event as described had never taken place, since her previous testimony had been used to prove that it was an actual occurrence. When, however, it was pointed out that the sentence received by the man was well within the statutory limits for automobile theft and violation of parole and that his criminal negligence toward her presumably had not been considered in the passing of the sentence, she seemed much relieved, considered the situation as a closed incident and actually continued so to regard it. Apparently, she was satisfied that no wrong had been occasioned by her "misstatements" and, hence, that her "mistaken" testimony had never actually won credence, which, in turn, implied for her the unreality of the original experience.

COMMENT

What might have been the outcome had these cases been again brought into court is only speculative. General experience, however, in similar cases suggests the not unusual development of "reasonable doubt" resulting from the recanting of testimony previously given by an otherwise credible witness and a consequent acquittal because of failure to prove again the guilt originally established. Whether any legal provisions can be made for "witness unreliability" of this character is a serious question, but at least recognition should be accorded to the possibility and the frequency of such psychologic behavior, as a measure of lessening the confusion occasioned by it.

Psychiatrically, any discussion of these two, or rather three, cases, since the two sisters were entirely independent of one another in the development of their reactions to the situation, constitutes a difficult problem. To elucidate the various psychologic processes entering into the final outcome would necessarily be so speculative as to be unwarranted. A day by day account of a highly detailed character would be needed to trace the steps by which the alteration of belief was achieved, and such a measure, in itself, might serve to bring about an entirely different end-result. Also, the data at hand in these cases are insufficient to permit more than a general consideration of the problem represented.

In this regard, however, attention may be directed to the fact that the experiences of the three girls are essentially identical in psychologic structure and represent the not unusual legal situation in which a female, after sexual usage, testifies first against the offending male and then, after a period of suffering, reverses her beliefs and attitudes, to testify sincerely in his behalf. This identity is manifest primarily in: (1) the highly pleasurable, exciting initial development of the experience; (2) the sudden complete transformation of this pleasurable situation into one of extreme terror, physical helplessness and pain, and (3) the final evolution into a situation of long-continued suffering and general helplessness.

In each instance, certain psychologic elements leading to the final outcome are to be found in common, and these may be summarized as:

1. General setting at defiance of authority and association with and participation in forbidden things.

2. A primary sexual relationship, illicit in character and marked by guilty, but pleasurable, participation.

3. Utilization of the female simply as a sexual instrument, without regard for an emotional return to her.

4. Brutality, direct, sadistic and physical, in the first case, and indirect and essentially psychic, in the second, despite the physical aspects.

5. Infliction of serious somatic injuries serving to constitute both an immediate physical threat and a long-continuing threat of future physical destruction.

6. Suffering experienced in common with the offending male, originating from common guilt and characterized for all parties by loss of freedom, personal helplessness, stigmatization and uncertainty concerning the future.

7. Intensely bitter, resentful public denunciation of the offender by the victim, with self-exculpation and overemphasis on the other's guilt.

That these common elements were the essential dynamic forces in the negation of the original testimony can only be presumed, but unquestionably they played a significant rôle in the course of events. The details of the processes by which they served their purposes are a problem that must be left to more extensive studies, since this report can direct attention only to the original situation and the final significant outcome, with some suggestions regarding the processes involved in these instances. Further studies of an analytic character should serve to clarify more fully the psychologic processes of retrospective falsification, suppression and repression, memory distortion, affect displacement and substitution, compensatory reactions, guilt reactions, self-exculpation, denial of reality and wishful thinking which are shown to a significant degree in the histories in these cases.

In this regard, an analogy may be drawn between the behavior reported in these cases and that shown in daily routine life in the repression, faulty recall and even distortion of unpleasant, disagreeable experiences, since essentially the same dynamisms are operative in both situations, though to different degrees. The more extreme character of the reactions in these cases as compared with that found in ordinary behavior may be attributed to the extreme character of the experiences.

In all probability, the initial psychic dynamism in these cases, as in instances occurring in daily life, was the primary repression of the unpleasant affects arising not only from the traumatic aspects of the experience but from the girls' own guilty pleasurable participation. Contributory to this was the peculiar situation in court, in which all three girls, in telling their stories and seeking to affix blame on their aggressors, were forced psychologically, as well as legally, to disclose their own guilty participation. Thus, the two little girls in telling of their nude dancing, wine drinking, singing and playing with the genitals

of the men, and the older girl in describing her intention of spending a night of illicit love-making, were declaring in essence: "All this I was doing to make my aggressor happy, and see what he has done to me." Yet by thus emphasizing the guilt of the men, the girls placed themselves in a definitely humiliating position, thereby giving rise to a compelling need for self-exculpation. This could be possible only in a totally different situation, since self-exculpation could be achieved only by the process of exculpation of others. Hence, repression of self-condemnatory feelings would necessitate repression of other related aspects and would require a total reorganization and reconstruction of the experience in a form more assimilable to the personality.

Also to be considered in this regard are the loss of physical intactness, the infections of long duration and the ever-recurring physical assault involved in the intravenous and intramuscular therapy for the two little girls, and the facial burns, the broken ribs and the injured arm and legs threatening to disfigure the older girl. These physically traumatic aspects of the experiences gave rise to an intense wish that these things would not and could not be so, that things would change completely. In response to this great need there developed the psychologic processes by which, step by step, there could be utilization of repressions, overemphasis of various elements in the experience and distortion of others, until finally there had been achieved a complete reconstruction of the entire experience in a form which could meet the compelling needs of the personality. In the case of the two children, one step in this process is clearly illustrated by their statement, "Ma didn't like those things," which progressed to "Ma wouldn't let those things happen."

Thus, shifting of responsibility to their mother for the realities of the occurrence was achieved, enabling them to avoid any necessity for relying on, or even utilizing, their knowledge of the actualities of their experience.

Similarly, the older girl summarized her psychologic treatment of the experience with great clarity by declaring it to be "utterly intolerable, one that could be imagined but not endured." By regarding the experience as imaginable but unendurable, she could give herself free rein to regard it as imaginary, utilizing the fact of her survival as proof of its imaginary character. But the fallaciousness of this apparently gave rise to her compulsive need to secure proof from external forces, manifested in her seeking a retrial for the purpose of establishing by formal legal processes the unreality of the desertion. Essentially, this constituted the same process of shifting responsibility for the realities of the experience as was employed by the two children in placing their reliance on their mother. Thus, her relief on being shown conclusively that the man had been punished only for offenses which she could readily recognize as real and which were not related to her becomes easily comprehensible. The prison sentence proved conclusively to her that the realities of the original situation were only those of automobile theft, violation of parole and an unavoidable accident, for which no one could be held responsible.

That many considerations other than those discussed entered into the final outcome in these cases is readily admitted, but the deficiencies of the data render further elaboration overspeculative.

DERMOID OF THE SPINAL CORD

Report of a Case in Which There Was Removal with Improvement

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Since there are few reported cases of epidermoid or dermoid tumor of the spinal cord, fewer in which operation was performed and still fewer in which improvement followed operation, it is considered important from a diagnostic and therapeutic standpoint to place this single case on record.

Gross [1] found reports in the literature of 19 cases of epidermoid or dermoid tumor of the spinal cord and added 1 case in which operation was performed by Dr. Percival Bailey, of Chicago. In a review of these cases, Gross stated:

> The tumors which are included in this group vary somewhat in their structure and in their relation to the spinal cord and its membranes. An analysis of the cases, including the one herein reported, reveals the following: of twenty cases, nine were in females, ten in males, and in one the sex was not stated. The youngest patient was an anencephalic monster who only survived a few hours, the oldest was sixty-four years of age. The greatest number fell in the third and fourth decades, in which there were eleven cases. The duration of symptoms on the whole was relatively long, averaging about ten years. One patient with a dermoid in the region of the cauda equina had had bladder disturbances for more than twenty years. In relation to the spinal cord, two tumors were extradural, ten were intradural, but extramedullary, six were intramedullary, one traversed the entire central canal beginning in the medulla oblongata, and in one the relations were not described. As to position, one tumor traversed the entire central canal; in one case tumors were disseminated throughout the subarachnoid space, seven were in the dorsal region, four in the dorso-lumbar region, three in the lumbar region, and four in the region of the conus and cauda equina.

Bostroem [2] expressed the belief that the epidermoids (pearly tumors) and dermoids have their origin in the embryonic inclusions of epidermal cells, and most authors have followed him in this opinion. In splitting off of the neurectoderm from the medullary plate, inclusions of epidermal cells may occur. These embryonic rests often possess potentialities for growth and differentiation. It is thought that the age in embryonic life at which the inclusion occurs determines more or less the position and structure of the resulting tumor. Tumors of simple structure in which epidermal appendages are absent are thought to have their origin in epidermal inclusions which occurred relatively early in embryonic life. These form the epidermoids, or true pearly

1. Gross, S. W.: Concerning Intraspinal Dermoids and Epidermoids, with Report of a Case, J. Nerv. & Ment. Dis. **80**:274-284, 1934.

2. Bostroem, E.: Ueber die pialen Epidermoide, Dermoide und Lipome, und die duralen Dermoide, Centralbl. f. allg. Path. u. path. Anat. **8**:2, 1897.

tumors. Inclusions at a slightly later period, from cells which give rise to hair follicles and glands, form the simple dermoids. It is possible also for these cell inclusions to give rise to more complex malformations, such as the teratomatous cysts of the spinal cord reported by Kubie and Fulton.[3] The congenital origin of these tumors is indicated by their occurrence in very early life in some of the cases reported and the long duration of symptoms in most of the others. The close relation between the epidermoids and the dermoids is revealed in their coexistence in the same patient in 3 cases.

There follows a brief résumé of the cases reported in which operation was performed. Verebely [4] reported a case in a girl aged 15 who had had a mass in the lumbar region from birth; at operation a large bilocular cyst was removed which proved to be a dermoid. Robertson and Ingham [5] removed a cholesteatoma from the lower dorsal and upper lumbar region of the cord, with subsequent benefit to the patient. Marinesco and Draganesco [6] performed laminectomy for removal of and intradural degenerated cholesteatomatous tumor. Salotti [7] recorded a case in which a large mass was localized by injection of poppyseed oil and removed from the lower dorsal and upper lumbar region. In Fraser's case [8] the operation was performed after injection of poppyseed oil. An epidermoid was removed at the level of the eighth dorsal vertebra. Melnikoff-Raswedenkoff [9] operated on a patient who succumbed; necropsy revealed an intramedullary spindle-shaped epidermoid at the level of the fifth and sixth dorsal vertebrae. Michelsen's patient [10] was operated on after injection of poppyseed oil; a tumor was observed at the level of the ninth dorsal vertebra; necropsy revealed that the tumor was attached to the pia on the dorsal aspect of the cord. Bailey's case was diagnosed as one of lesion of the spinal cord; two operations yielded a good result.

Naffziger and Jones [11] reported 4 cases of dermoid tumor of the spinal cord, in 3 of which the diagnosis was tumor of the cauda equina and in the fourth a dermoid tumor of the cauda equina. From the standpoint of localization, operative procedure and subsequent improve-

3. Kubie, L. S., and Fulton, J. F.: Clinical and Pathological Study of Two Teratomatous Cysts of the Spinal Cord, Surg., Gynec. & Obst. **47**:297-311, 1928.

4. von Verebely, T.: Ein Fall von intravertebraler Dermoidzyste, Virchows Arch. f. path. Anat. **213**:541-544, 1913.

5. Robertson, W. E., and Ingham, S. D.: Case of Cholesteatoma of the Spinal Cord, Pennsylvania M. J. **19**:408-413, 1916.

6. Marinesco, G., and Draganesco, S.: Kyste épidermöide cholésteatomateaux de la moelle épinière, Rev. neurol. **40**:338-355, 1924.

7. Salotti, A.: Dermoid del midolo spinale, Arch. ital. di chir. **19**:135-157, 1927.

8. Fraser, J. A.: Cystic Dermoid Tumor of the Spinal Cord, Surg., Gynec. & Obst. **51**:162-168, 1930.

9. Melnikoff-Raswedenkoff, N. F.: Ueber epidermoide und dermoide Cholesteatome des Grosshirns und Rückenmarks, Virchows Arch. f. path. Anat. **279**:702-723, 1931.

10. Michelsen, J.: Cholesteatome des Rückenmarkes, Deutsche Ztschr. f. Nervenh. **127**:123-130, 1932.

11. Naffziger, H. C., and Jones, O. W., Jr.: Dermoid Tumors of the Spinal Cord, Arch. Neurol. & Psychiat. **33**:941-958 (May) 1935.

ment these 4 cases represent the largest group reported. How the clinical diagnosis of dermoid tumor was made in the fourth case was not stated. In 3 of the 4 cases operation resulted in complete removal of the lesion, and in the fourth, in nearly complete removal with marked improvement.

Therefore, in 11 of the 24 cases reported in the literature to date operation was performed: In 6 definite improvement was reported; in 3 no statement was made as to the result; and in 2 autopsy reports were appended. Of the cases reported, the percentage in which improvement from operation was certain is 25; if the 3 cases are added in which no definite statement was made regarding the postoperative course, the figure is 37 per cent. This is a poor showing as compared with the operative result obtained with many neoplasms of the spinal cord. This may be due in part to an error in diagnosis, as a result of which the patient was not operated on early, and in part to the nature of the lesion—extramedullary in many instances, but frequently intramedullary.

The long duration of symptoms due to compression of the cord, which is illustrated in the case reported here, militates as a rule against full recovery of function. Changes in the cord resulting from simple compression together with interference with blood supply at the site of the lesion, are to be reckoned with.

REPORT OF CASE

A. W., aged 38, was admitted to the Veterans Administration Facility, Dutchess County, N. Y., on Nov. 30, 1934, with the complaint of pain in the right thoracic region and the spine at about the level of the eighth dorsal vertebra and progressive weakness in both legs.

While the patient was serving as a farrier at Saint-Nazaire, France, in 1917, a bale of hay fell against his back, causing pain in about the middle of the spine. Later in the same year, while shoeing a mule, he was pushed against the wall forcibly, but did not strike his back. This produced pain in the back at the same place as before (the right thoracic region at about the level of the eighth dorsal vertebra) for two weeks. In May 1918 he was kicked by a mule, which caused him to fall on his face; this resulted in almost continuous pain in the back. By October 1918 he was using every precaution against jarring the body, as in friendly scuffles with fellow soldiers, because it produced a sharp pain in the back. Strenuous effort, such as lifting heavy loads, caused pain in the back. Owing to his disability, he was transferred to a "rolling kitchen" in November 1918, where he found that when he was standing or sitting in the conveyance jolts and jars were transmitted that were unbearable. He usually walked or stood on the balls of the feet to absorb pain-producing jolts. Because of his continuous complaint of pain in the back, extending at times to the hips and upward to a spot between the shoulders, he was hospitalized in 1918, while in the Meuse-Argonne sector; he said, however, that nothing abnormal was found. In 1918 he was transferred to a band to play the saxophone, but was not successful in this because taking a deep breath caused pain in the right thoracic region. He was transferred to duty in caring for race horses and in developing a circus. From childhood he had been a good rider, but found himself handicapped because each time he "jumped a horse" he experienced a severe gripping pain in the back. When he contracted a cold, coughing efforts produced the same pain. In 1920 he returned to the band, but only to repair instruments. At this time, whenever he suffered pain in the back an erection occurred. He con-

tinued on light duty and in 1921 returned to the United States, when for the first time he felt numbness in the toes, first of the left and then of the right foot. While still in the army he was again admitted to an infirmary in Maryland, with the complaint of pain in the back, encircling the abdomen at the lower border of the ribs. He gained weight and in general felt better in the warm climate.

In 1923, after discharge from the army he obtained work as a blacksmith, but lifting caused such pain and weakness in the legs that he had to give up the work. An attempt at running a streetcar was unsuccessful because standing on the platform, with consequent jarring, produced pain. Occasionally pain appeared spontaneously. He did light repair work until 1924, when he joined the Marine Corps. He attempted to box, but soon felt such terrific pain in the back that he gave up this sport. He then served in the band as a repairman and had "easy duty" in Cuba, which improved his general condition but did not cure the pain. In 1928 he was again hospitalized, but nothing was found to account for the pain and weakness of the left leg. He remained on light duty until May 1928, when he was discharged. In 1929 he noted reduction in the force of the urinary stream. A strenuous effort to expel urine rapidly produced pain in the back and right upper abdominal region. In October 1930 he noticed that he stumbled over any little obstruction. Hard work produced numbness of the legs, and in the morning the numbness and clumsiness were more pronounced. Later in the day he seemed to regain his balance. On October 25, owing to unsteadiness, he fell, placing his right arm on an elevator drum in motion. This crushed and destroyed his right arm, necessitating amputation just below the shoulder joint. In 1931 walking long distances caused increase in pain and numbness in the legs. During 1932 the pain became worse, and the speed of walking decreased. Motor power became progressively worse. During 1934 there was difficulty in starting the flow of urine. Reclining, as well as coughing, sneezing or straining at stool, produced pain.

Neurologic Examination.—Examination on Dec. 14, 1934, revealed that the patient was well nourished and well developed. There was an amputation stump at the upper third of the right arm. Station was affected. With both feet together and the eyes closed the patient swayed in all directions and fell if unassisted. He walked alone slowly and carefully, scuffing and carrying the left foot in an everted position. He had sufficient power to climb on the examining table but suffered severe pain, as evidenced in his facial expression. While lying on his back he elevated the extended right leg 3 feet (91 cm.), but could scarcely raise the left leg. Power in the upper extremities was preserved. The tendon reflexes were increased in the lower extremities, those on the left being more active than those on the right. A Babinski sign was definite on the left and suggested on the right. The cremasteric and lower abdominal reflexes were absent, while the upper abdominal reflexes were active. The sensory status is shown in the accompanying diagram (fig. 1). Position sense was greatly affected in the left lower extremity, up to and including the knee joint.

On December 17 a spinal manometric test was performed with a water manometer. Normal respiratory movements were absent. Light momentary compression of both jugular veins in the neck caused no rise in pressure, but each time this was done sudden, sharp pain was felt in the lower thoracic region on the right. A strong straining effort effected a slight rise in the fluid level and, at the same time, induced pain. Several coughing efforts raised the pressure to 200 mm., and then to 240 mm. The fall in pressure was slow. Deep compression of both jugular veins for ten seconds raised the pressure from 190 to 300 mm. During this time the patient groaned with pain and strained a little. In thirty seconds the level fell to 200 mm. and remained there. With the level at 190 mm., abdominal straining

raised the level to 400 mm.; it fell slowly, taking thirty seconds to reach 200 mm. After the removal of 7.5 cc. of cerebrospinal fluid the level fell to zero, and the patient suffered severe pain, which was referred to the lower ribs. These findings pointed to a subarachnoid block and substantiated the diagnosis of an expanding lesion in the vertebral canal.

The jolts, jars and forced expiratory efforts which the patient experienced could easily have produced pain as the result of a lesion attached to, or otherwise compromising, a nerve root. Forced respiratory movements, such as those involved in playing a wind instrument

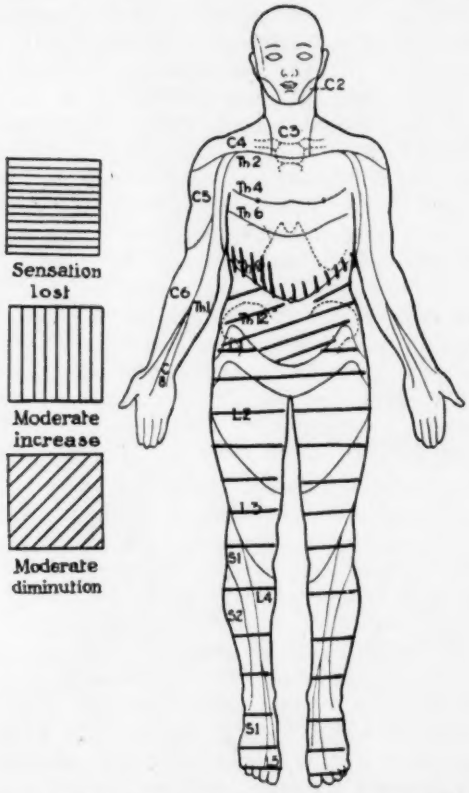


Fig. 1.—Diagram showing the sensory status of the patient on examination in December 1934.

or in lifting heavy objects, changed the relations of the intracranial and the intraspinal pressure and could easily have produced pain such as the patient asserted he suffered. The results of the spinal manometric test bore out this contention. I have never seen light compression elicit radicular pain so exquisitely, which in this case was always referred to the distribution of the eighth dorsal root on the right. The patient was an extroverted person. At no time did he magnify his symptoms or complaints. On cross questioning, he could not be swerved from his story of symptoms. Therefore, one is forced to conclude that the existing lesion had its incipiency at least in 1917.

Laboratory Studies.—The blood picture, the coagulation time, the blood chemistry and the results of urinalysis were normal. The Wassermann reaction was negative for both the blood serum and the spinal fluid. The total protein content of the spinal fluid was 86 mg. per hundred cubic centimeters of fluid (the normal being 50 mg.); the globulin content was estimated to be one plus. Roentgenographic examination of the spine showed that the right pedicle of the eighth thoracic vertebra was not as distinct as the others.

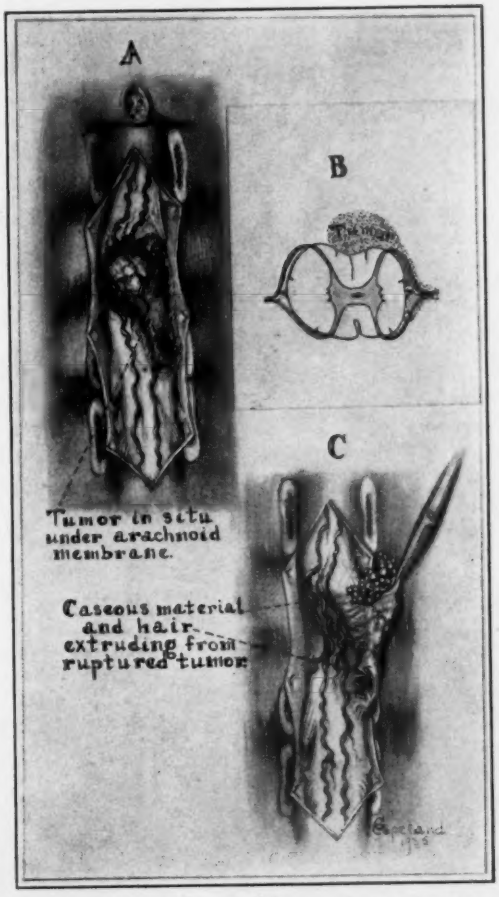


Fig. 2.—Drawings showing the position and appearance of the tumor at operation.

Preoperative Diagnosis.—The diagnosis was intradural meningioma in the right dorsolateral region, under the eighth thoracic lamina.

Operation.—On December 19 laminectomy was performed. With the patient under anesthesia induced with avertin and ether, the spines and laminas of the eighth and ninth, and a part of the tenth, thoracic vertebra were removed. A sense of resistance was then felt through the dura at the eighth thoracic level. When the dura was opened, a "pearly" tumor, exactly dorsal in position and measuring 1.5 cm. in width, length and depth (fig. 2), was exposed. Continuous with it was

a prolongation downward along the right dorsolateral surface of the cord for a distance of about 3 cm. This portion was scarcely 0.5 cm. in width as it presented dorsally. It was of softer consistency, and in its distal half was a group of light brown hairs, about 2 cm. in length. These were readily seen through the arachnoid membrane and the capsule of the tumor. The lower end of the tumor was freed from the cord without disturbing the blood supply or pial investment. This part of the tumor was soft, contained caseous material and had to be removed piecemeal. There was a prolongation of the lesion at about the eighth dorsal root.

Fig. 3.—Structure of the wall of the cyst. At the upper edge is a well demarcated epidermal border. In the loose fibrous tissue below are occasional hair follicles. Hematoxylin and eosin stain; × 150.

This was clipped with two silver clips and cut free. Only one vessel of the cord entered the tumor. This had to be clipped to control hemorrhage and to allow for removal of the tumor. The large, round, dorsally placed portion of the tumor was removed easily, but a small lateral portion extended upward, wrapped itself about the dentate ligament and assumed a right ventrolateral position. No bleeding was encountered during the intradural manipulations. When the tumor was removed a marked indentation of the spinal cord was evident. This slowly became less

evident as the cord tended to assume its normal position. The dura was closed with interrupted black silk sutures; the muscle and deep fascia were closed with catgut sutures, and the superficial fascia and skin, with interrupted black silk sutures. The wound healed by primary union.

Tumor.—Grossly, the specimen consisted of an irregular oval, saclike structure, approximately 3 cm. in length and 1.5 cm. in width. The outer surface

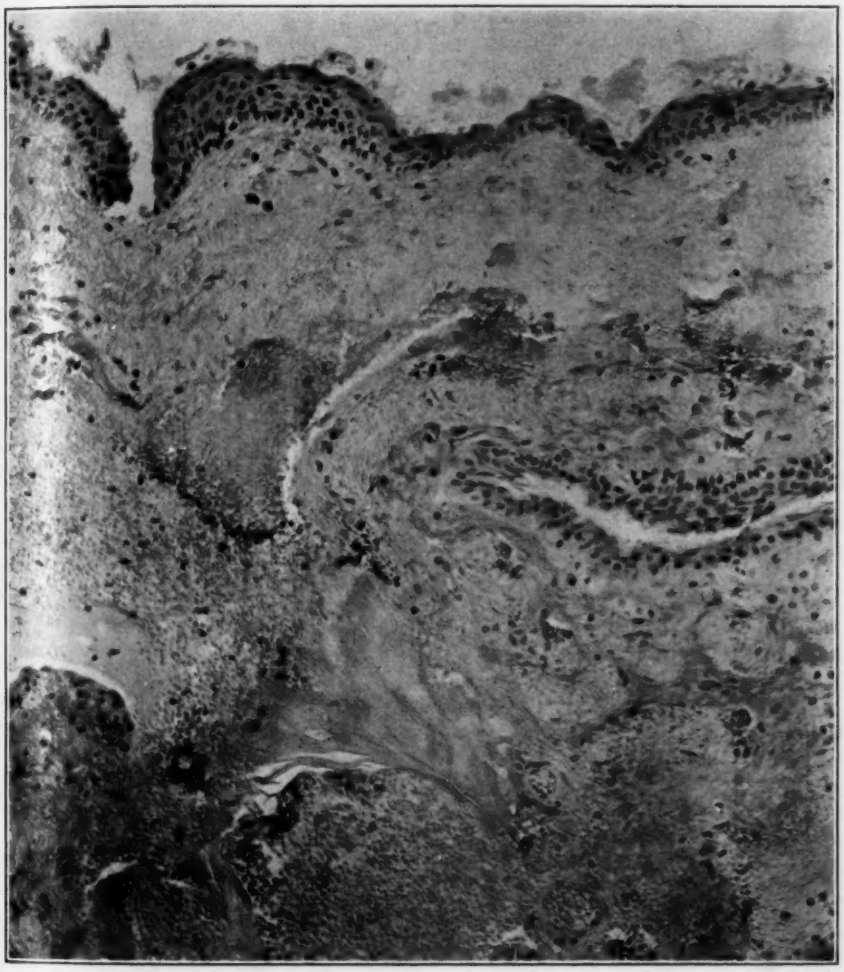


Fig. 4.—Higher magnification of the epidermal lining of the sac shown in figure 3. Hematoxylin and eosin stain; × 350.

appeared to be of tough fibrous tissue, on the surface of which were several small blood vessels. Within the collapsed sac there remained a small quantity of soft, sebaceous, yellow material and numerous white hairs. The inner surface of the sac appeared to be of more delicate structure and suggested a serous surface.

Microscopically, the specimen consisted of fairly dense fibrous and collagenous tissue, on one border of which was a sharply demarcated epidermal border consist-

ing of several layers of epithelial cells. In the looser fibrous tissue separating the epithelium from the collagenous capsule were numerous hair follicles. Sweat glands and smooth muscle were not observed in the sections studied, nor were there any more complicated structures The pathologic diagnosis was dermoid cyst (figs. 3 and 4).

Course.—After operation the patient had relief from pain but was rendered paraplegic. He could not void, and sensation in all modalities was lost up to the tenth dorsal dermatome on the left side and to the eighth dorsal dermatome on the right. The left patellar reflex was active and the right just perceptible; the achilles reflex was questionable on both sides. A Babinski response was obtained bilaterally. Two weeks later, when the legs were flexed at the knees they slid down on the bed slowly, a slight return of muscular tone and power thus being shown. Position sense was present in the left knee joint, and deep pain sense returned in the right great toe. One month after operation it was found that the patient had regained motor power in both thighs, but he still had to be catheterized. He could sit up in a wheel chair for several hours and described various subjective symptoms in the lower part of the abdomen and legs "like returning sensation." Six weeks later there were return of motor power in both lower extremities, a lower sensory level on both sides and a slight return of bladder control. The Babinski response was less easily elicited. From that time, improvement has been gradual; at the time of writing, the patient can walk with the aid of a walking machine; motor power is increasing; spasticity is becoming steadily less, and vesical and rectal control are practically normal. The sensory level is less marked. Position sense is lost up to and including the knee joints, which accounts in a large part for the delay in walking.

SUMMARY

A case is reported which represents histologically a classic intradural dermoid tumor of the spinal cord, historically a lesion of seventeen years' duration, neurologically progressive dysfunction of the spinal cord over a long period and surgically a satisfactory result, all the attendant circumstances being considered.

33 East Sixty-Sixth Street.

Technical and Occasional Notes

MODIFICATIONS IN TECHNIC FOR USE OF THE HORSLEY-CLARKE STEREOTAXIC INSTRUMENT

FRANK HARRISON, PH.D., CHICAGO

In this paper are presented certain changes in technic for the use of the stereotaxic instrument (Horsley and Clarke [1]) which have been introduced since the publication of a former paper dealing with this subject (Ranson [2]).

Rotation of the vertical needle carrier in the sagittal plane is sometimes advantageous in order to insert the needle or electrode into the brain of an experimental animal in a direction other than the perpendicular plane of the conventional machine. This has been accomplished in this laboratory by pivoting the vertical needle carrier so that it can be rotated in the sagittal plane to any desired angle up to 45 degrees from the vertical position. The construction of this pivoted needle carrier can readily be understood from the photographs reproduced in the accompanying figure. The coordinates employed for locating any point in the interior of the brain when the pivoted needle carrier is used can be derived from the regular rectilinear coordinates of the Horsley-Clarke instrument by simple trigonometric formulas.[3]

Lesions of large size can best be made with a bipolar electrode similar to that which has previously been used for stimulation (Ingram and his co-workers [4]), except that the bare tips of the two constituent wires are separated by a distance of 2 mm. along the long axis of the electrode. The larger wire extends to the tip of the electrode and serves as the anode; the smaller wire, ending 2 mm. short of the tip, is the cathode. The anodal and cathodal lesions fuse, destroying a cylindric area about 3 mm. long. With a direct current of 3 milliamperes for sixty seconds the cylindric area destroyed has a diameter of about 1.5 mm. Increase in the strength or duration of the current will not much enlarge the lesion. The area of destruction can best be extended by making additional lesions so close to the first and to each other that they will fuse into one.

The direct current used in making the lesions was formerly taken from a 45 volt B battery, but this proved unsatisfactory for the production of large lesions; the necessary amperage is now drawn from a 110 volt direct current outlet. The

This study was aided by a grant from the Rockefeller Foundation.

From the Institute of Neurology, the Northwestern University Medical School.

1. Horsley, V., and Clarke, R. H.: The Structure and Function of the Cerebellum Examined by a New Method, Brain **31**:45, 1908.

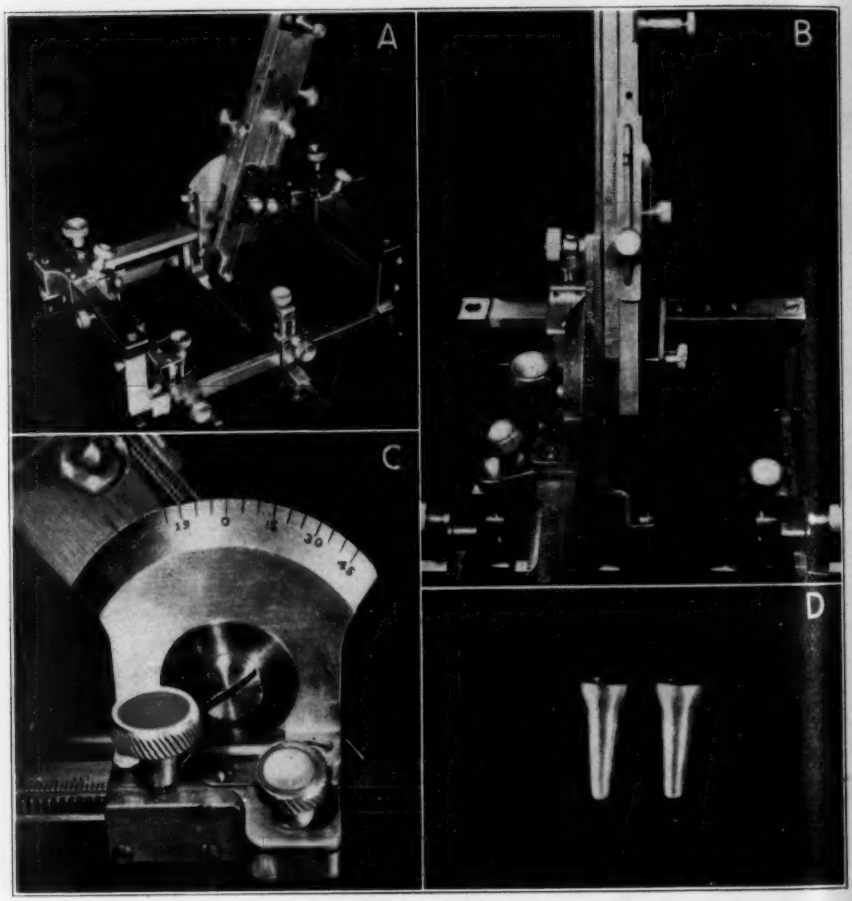
2. Ranson, S. W.: On the Use of the Horsley-Clarke Stereotaxic Instrument, Psychiat. en neurol. bl. **[38]**:534, 1934.

3. Details concerning these formulas and their use in the calculations will be furnished on request.

4. Ingram, W. R., and others: Results of Stimulation of the Tegmentum with the Horsley-Clarke Stereotaxic Apparatus, Arch. Neurol. & Psychiat. **28**:513 (Sept.) 1932.

components of the circuit are in series and consist of: a 100,000 ohm standard untapered radio volume control, a 30,000 ohm volume control, a milliammeter registering to 15 milliamperes, the electrodes for insertion in the brain, and a switch.

Slitting the lower margin of the ear has been abandoned because it was frequently followed by infection and was found not to be necessary. Instead, the rim at the outer end of the ear plug is firmly grasped with a hemostat, and the plug



A, oblique view of the Horsley-Clarke stereotaxic instrument from the left; *B*, view from the front, showing the rotating needle carrier; *C*, view of the pivot and scale for the rotating needle carrier, and *D*, new type of ear plugs for the monkey, natural size.

is directed downward and forward into the external auditory meatus. This is easily accomplished without force if the pinna is pulled slightly upward at the time the plug is inserted. To insert the ear bar into the conical depression of the plug, use is made of a blunt probe. The tip of the probe is placed in the hollow of the ear plug and the tip of the ear bar slipped in along the probe until it is seated;

then the probe is withdrawn. The entire procedure is easily learned with a little practice, and the inevitable bleeding with the older method is avoided.

Rhesus monkeys have heads which are of uniform shape and well suited for the use of the Horsley-Clarke instrument. In this laboratory, however, localization has not been as accurate in the monkey as in the cat. This has been due in part, at least, to the use of the special frontal plate recommended for the monkey by Horsley and Clarke. This plate is secured in place by a screw which presses backward on the forehead. The pressure of this screw draws the instrument forward on the animal's head a variable amount, depending on the degree of pressure exerted and the ease with which the external auditory meatus can be pulled forward. For this reason, the use of this special frontal plate has recently been abandoned in this laboratory. The frontal plate designed for the cat is is entirely satisfactory for use with the monkey.

The ear plugs designed for use with the monkey (Ranson [2]) have been found to be too long. In their place, use is now made of the shorter straight plugs illustrated in the figure (*D*). Their total length is 15 mm., and they are reproduced in the figure at approximately their true size.

Obituaries

ALFRED WALTER CAMPBELL, M.D., CH.M.
1868-1937

In a recent survey of existing knowledge concerning the finer structures of the cerebral cortex [1] Lorente de Nó concluded that the most satisfactory studies of architectonics published to date were those of Alfred W. Campbell, issued in 1905 under the title "Histological Studies of the Localisation of Cerebral Function." He remarked:

> The only really good cytoarchitectonic pictures are those of Campbell, who—let me put it in capital letters—HAS BEEN THE ONLY CYTOARCHITECTONIST WHO HAS DESCRIBED FACTS AND ONLY FACTS. The German cytoarchitectonist has mixed facts with theory in such a manner that nobody can tell where facts end and theories begin. I must state that there are perhaps no more than a dozen photographs out of hundreds in which the layers of the cortex have been properly and consistently labeled. On the other hand, Campbell's ink drawings, beside being good, are easily reproduced.

A few months ago I published a short history of cytoarchitectural studies of the cortex,[2] and at that time I attempted to reach Dr. Campbell in order to send him a reprint. The paper was published on Nov. 4, 1937, and was sent immediately to Australia, where Dr. Campbell had been listed in 1936 as being still in practice. A gracious reply was received from Dr. Campbell's daughter, who stated that her father had passed away in his house on McQuarrie Street, in Sydney, on Nov. 4, 1937. The *Medical Journal of Australia* carried a full obituary of Campbell under the date of Jan. 22, 1938, with a photograph and bibliography. The following details concerning his remarkable career are taken largely from this source, but also from private information.

Born Jan. 18, 1868, on his father's station at Cunningham Plains, near Harden, Australia, Alfred Campbell received his early education under the headmastership of the son of Robert Southey, the English poet, at Oakland School near Mittagong. He left Australia in 1885 to

1. Lorente de Nó, R.: Architectonics and Structure of the Cerebral Cortex, in Fulton, J. F.: Physiology of the Nervous System, New York, Oxford University Press, 1938, pp. 291-327.

2. Fulton, J. F.: A Note on Francesco Gennari and the Early History of Cytoarchictectural Studies of the Cerebral Cortex, Bull. Inst. Hist. Med. **5**:895-913 (Dec.) 1937.

enter the medical school at Edinburgh, Scotland, and in 1889 received the M.B. and Ch.M. degrees, with honors. His attention had early been drawn to mental disease, and he soon became one of that still small band who believe that the study of the structure of the brain and its aberrations may one day lead to a deeper understanding of the deranged mentality. He visited various English asylums and later went to Vienna, Austria, where he was largely influenced by Krafft-Ebing; on leaving Vienna he proceeded to Prague, Czechoslovakia, where he served for a time on the staff of the state asylum of the metropolis. On returning to England in 1892, he obtained the degree of Doctor of Medicine at Edinburgh for a thesis entitled "The Pathology of Alcoholic Insanity" and was awarded a gold medal. He then accepted a dual appointment as staff member at the Lancashire County Asylum and director of the pathologic laboratory at the Rainhill Asylum, Liverpool, England. In these capacities he had opportunity to see extraordinarily varied clinical material. The Rainhill Asylum became affiliated under his direction with the University of Liverpool and soon became a mecca for students and visitors from all parts of the world.

While at Liverpool Campbell became associated with Charles Sherrington and under this stimulus began his epoch-making studies on the structure of the cortex, to which reference has already been made. In 1901 Grünbaum and Sherrington had published their physiologic studies on the electrical excitability of the cerebral cortex in higher apes. Campbell had the opportunity of seeing these experiments, and the brains of many of the anthropoids were turned over to him for histologic study. In the three years between 1900 and 1903 Campbell accomplished the almost incredible task of cutting serial sections of each of 25 brains, staining his sections alternately for cells and for fibers; he prepared the material for publication in monographic form by the end of 1903. The material was too extensive even for the *Philosophical Transactions of the Royal Society of London*; through Sherrington's influence, however, a grant was made by the society, and the treatise was published by the Cambridge University Press as a separate monograph. Campbell was an excellent draftsman, and while many of his now classic plates were drawn by himself, he also had the assistance of his colleague, Dr. A. C. Wilson, of the Rainhill Asylum. Among other things, he defined the motor area as well as the premotor area on the histologic basis which is now widely recognized. The premotor region was designated the "intermediate precentral area." He had opportunity to examine brains of patients who had undergone, sometime prior to death, amputation of one or more limbs, and he was able to show that atrophy in the motor region was restricted to the cells of Betz. He also examined the postcentral region in cases of tabes

dorsalis. He recognized all the principal regions which had then or have since been recognized as having physiologic significance.

After returning to Australia Dr. Campbell published a number of additional papers on localization of cerebral function, but it is to be regretted that the responsibilities of private practice drew him away from investigative work and precluded his making the large contribution to scientific neurology which he might well have made. Campbell returned to Australia in 1905, before his book was actually off the press. He settled at once in practice at Sydney and continued until his retirement early in 1937, as one of the most distinguished and respected practitioners in Australia. In 1906 he married Jennie, daughter of David Mackay, of Wallen Been Station, adjoining that on which Dr. Campbell was born. There were two daughters. In 1914 Campbell volunteered for war service and was sent to Egypt. On returning to Australia he was appointed to the Military Hospital at Randwick, a post which he held at the time of his death. He was consultant neurologist to the Royal Alexander Hospital for Children, the Coast Hospital and the Department of Repatriation in Australia.

Campbell was a man of powerful Scottish physique, who had always taken a keen interest in sport, especially golf and cricket, and was also a good marksman, a keen and well informed ornithologist and a botanist of distinction. He had a large library of works in the field of general history as well as in the history of medicine and science. American neurologists extend their sympathy to his family and to all his colleagues in Australia.

JOHN F. FULTON, M.D.

News and Comment

FELLOWSHIP AWARDS

The National Committee for Mental Hygiene announces the following fellowship appointments for one year's training in extramural psychiatry. Under a grant from the Commonwealth Fund: Dr. Grace E. McLean, of the Pilgrim State Hospital (Brentwood, N. Y.), to the Cleveland Child Guidance Clinic; Dr. John A. Rose, Cornell Student Health Service, to the Philadelphia Child Guidance Clinic; Dr. John Russell, of the Osawatomie (Kan.) State Hospital, to the Los Angeles Child Guidance Clinic; Dr. Rex E. Buxton, of the Iowa Psychopathic Hospital, to the Judge Baker Guidance Center; Dr. W. B. Curtis, now on the neurologic and neurosurgical service at the Bellevue Hospital, to the Mental Hygiene Clinic at Louisville, Ky. Under local provision: Dr. William L. Holt Jr., of the Worcester State Hospital, to its Child Guidance Clinic; Dr. Norman Westlund, of Traverse City (Mich.) State Hospital, to the Children's Center at Detroit.

Abstracts from Current Literature

Physiology and Biochemistry

BRAIN POTENTIALS DURING SLEEP. H. BLAKE and R. W. GERARD, Am. J. Physiol. **119**:692 (Aug.) 1937.

Blake and Gerard studied the brain potentials of young adults during normal night sleep, afternoon napping, postinsomnia sleep and, in 1 case, hypnosis. Depth of sleep was independently determined by the duration of a fixed sound required to awaken the subject (response to a question), by movement, by respiration and the like, and an orthodox curve for depth of sleep for the night was so obtained. Potential patterns correlate with the depth of sleep not only over long periods but, in most cases, rather accurately over short swings in time. Deep sleep is regularly associated with a large regular potential wave at a frequency of from ½ to 3 a second; lighter sleep, with feeble irregular potentials or with the 10 a second rhythm. The results are interpreted in terms of excitation levels of cerebral neurons and of the play of nerve impulses on them. With low excitation a slow rhythm is manifest; with stronger excitation, a faster rhythm, and in transition between these states asynchrony prevents the manifestation of any regular beat.

EDITOR'S ABSTRACT.

ELECTROENCEPHALOGRAM OF SCHIZOPHRENICS DURING INSULIN HYPOGLYCEMIA AND RECOVERY. H. HOAGLAND, M. A. RUBIN and D. E. CAMERON, Am. J. Physiol. **120**:559 (Nov.) 1937.

Hoagland and his associates made electroencephalographic records during 35 treatments of 6 schizophrenic patients with insulin. Electrical brain waves after large doses of insulin show a progressive decline in the frequency of the alpha wave (Berger rhythm) of about 40 per cent, which parallels with a time lag of about thirty minutes the declining curve for blood sugar. Sugar injected during coma restores the frequency along a smooth curve. The present data, with other evidence, are in accord with the view that alpha frequencies are directly proportional to the rate of carbohydrate metabolism in the cortical cells producing the rhythm.

EDITOR'S ABSTRACT.

THE EFFECT OF ARTIFICIALLY RAISED METABOLIC RATE ON THE ELECTRO-ENCEPHALOGRAM OF SCHIZOPHRENIC PATIENTS. M. O. RUBIN, L. H. COHEN and H. HOAGLAND, Endocrinology **21**:536 (July) 1937.

Rubin and his associates gave intravenous injections of thyroxin daily to 4 patients with schizophrenia. The initial daily dose was 2.5 mg.; this was increased to 3.75 mg. for approximately four weeks. Three tests were made weekly on each patient during an experimental period of two and one-half months. The effect on the alpha frequency in the electro-encephalogram of artificial increases in basal metabolic rates was observed. It is inferred that an increase in the basal metabolic rate involves an increase in the rate of cerebral respiration. In 3 of the patients the alpha frequency was increased by from 4.9 to 17.2 per cent when the basal metabolic rate was increased by from 26.5 to 47.7 per cent. The fourth patient showed an initial increase in alpha frequency accompanying an increase in the basal metabolic rate; after about a week, despite a continued high metabolic rate, the alpha frequency fell to the prethyroxinization level. In general, increase in the metabolic rate was associated with a rise in alpha frequency. A constant high level for both these variables was maintained during thyroxin medication, despite an increase in dose and the continuation of thyroxin, and was maintained

for a long period after thyroxin administration was discontinued. The data obtained in this investigation lend further weight to the hypothesis that there exists a quantitative relationship between the alpha frequency and the carbohydrate metabolism of the brain. PALMER, Philadelphia.

THE EFFECT OF HYPOGLYCEMIA ON THE METABOLISM OF THE BRAIN. J. E. HIMWICH and J. F. FAZEKAS, Endocrinology **21**:800 (Nov.) 1937.

Himwich and Fazekas studied the effect of hypoglycemia on the dextrose and oxygen exchanges of brain and muscle. When under amytal anesthesia, fasting dogs were given insulin in doses of 1 unit per kilogram every two hours until the respiratory and heart rate slowed markedly. The cerebral exchanges varied directly with the level of the blood sugar. With the arterial blood sugar between 110 and 62 mg. per hundred cubic centimeters, the utilization of dextrose by amytalized animals was 13.1 mg. per hundred cubic centimeters, and that of oxygen, 9.3 volumes per cent. When the values for blood sugar varied from 46 to 25 mg., the uptake of dextrose was 12.5 mg. per hundred cubic centimeters, and that of oxygen, 7.99 volumes per cent. When the blood sugar was reduced to values of from 22 to 7 mg., the absorption of dextrose decreased to 3 mg. per hundred cubic centimeters, and that of oxygen, to 3.8 volumes per cent. The store of carbohydrate in the brain, though small, is utilized during intense hypoglycemia and therefore probably supplies the material for oxidation. The fact that hypoglycemia is maintained for some time before the rate of oxygen consumption falls may also be attributed to utilization of intrinsic cerebral carbohydrate. Intravenous injection of dextrose during hypoglycemia restores the oxygen consumption of the brain to 9.14 volumes per cent. The observations are in marked contrast to those obtained simultaneously for muscle. When the utilization of dextrose fell from 7.6 to 1.7 mg. per hundred cubic centimeters during hypoglycemia, the values for oxygen were 6.91 and 6.04 volumes per cent, respectively. The metabolic effects of deprivation of dextrose are reversible at any level of the blood sugar if the animal is still capable of adequate respiratory and cardiac movements. It was found that amytal narcosis in their experiments was not a significant factor in the production of cerebral metabolic changes. PALMER, Philadelphia.

THE NATURE OF TOLERANCE TO ETHYL ALCOHOL. HENRY NEWMAN and JOHN CARD, J. Nerv. & Ment. Dis. **86**:428 (Oct.) 1937.

The generally accepted belief that an increased tolerance for alcohol results from its continued use has never been scientifically verified. Possible explanations for such an increased tolerance, if it exists in the habitué, include: (1) delayed absorption from the gastrointestinal tract; (2) an increased rate of metabolism (destruction) of alcohol, and (3) decreased sensitivity of the nerve cells to alcohol. Newman and Card studied the problem in dogs. They discovered that in dogs habituated for thirteen months to a daily dose of 6.8 cc. of alcohol per kilogram of body weight the concentration of alcohol in the blood following oral administration rose faster and reached a higher maximum than it did in nonhabituated dogs. Absorption is thus faster, and not slower, in the habitué. This is in accord with the findings of most other workers. Habituated dogs, however, showed a more rapid emptying time of the stomach than did nonhabituated dogs. The authors found that alcohol administered intravenously disappeared from the blood at almost the same rate in habituated and in nonhabituated animals. Alcohol given by mouth disappeared less rapidly from the blood of nonhabituated dogs, a fact attributable to the slower absorption in these animals. It was also found that in a given series of dogs alcohol is metabolized as rapidly before as after habituation. It was demonstrated that habituated dogs can be anesthetized by the same concentration as animals used as controls, but that they show more rapid recovery from the anesthesia than do nonhabituated dogs. Habituated dogs thus seem to

have a greater tolerance to concentrations less than anesthetic in degree. The basis for this tolerance to smaller concentrations has not yet been determined. Whether it is a changed permeability of nerve tissues, an increase in cellular tolerance or psychomotor compensatory mechanisms is not known.

MACKAY, Chicago.

REMOVAL OF RIGHT OR LEFT FRONTAL LOBES IN MAN. GEOFFREY JEFFERSON, Brit. M. J. **2**:199 (July 31) 1937.

Eight cases of excision of the frontal lobe for tumor are reported in detail. The entire lobe was not removed, but only the part anterior to the motor convolution. In 3 instances the operation was on the left side. Patients who show no mental alteration before operation are not affected mentally by removal of the frontal lobe. The left lobe can be removed as well as the right, for neither is dominant. Higher cerebral functions are not localized in any one small area. Not until large areas of brain, such as both frontal lobes, are removed does mental impairment become obvious.

ECHOLS, New Orleans.

Neuropathology

THE ASTROCYTOMAS. B. J. ALPERS and S. N. ROWE, Am. J. Cancer **30**:1 (May) 1937.

Alpers and Rowe analyzed a large group of astrocytomas in an effort to classify them histologically and to correlate their histologic with their clinical features. Division of the astrocytomas into fibrillary (solid and cystic), giant cell and cellular groups indicates the great preponderance of the fibrillary group and makes possible in the majority of instances a safe prediction of the course which the tumor will take. In general, tumors of the fibrillary and cystic groups grow slowly, and follow correspondingly slow clinical courses. The piloid group of fibrillary astrocytomas, while benign histologically, seems to be less benign clinically. Tumors of the giant cell and cellular groups grow more rapidly and correspondingly follow a more rapid clinical course than the fibrillary astrocytomas. Most of the fibrillary astrocytomas are represented by the diffuse, interlacing neuroglial carpet, which simulates the neuroglial arrangement in the normal white matter. The reason for the difference in appearance of these slowly growing tumors must remain at present a matter of speculation. Granting that the preponderance of fibrils in fibrillary astrocytomas is due entirely to their formation by the cells, the stimulus for their heavy deposit in some tumors as compared with that in others is still not evident, or the reason that some fibrillary astrocytomas develop as diffuse and others as piloid types, all of them being the result presumably of the same cell, the fibrillary astrocyte. In all the fibrillary tumors it is possible to see protoplasmic, as well as immature, types of astrocytes. The cellular form of astrocytoma is in reality the protoplasmic type, but even in this tumor there is some fibrillar formation. Since it is not clear whether the lack of fibrils is due to the presence of protoplasmic astrocytes or to immature cells, it is deemed best to refer to this tumor as a cellular astrocytoma. Similarly, there is little doubt that the giant cell astrocytomas constitute a group in themselves. In appearance and structure they are quite different from the other groups.

EDITOR'S ABSTRACT. [J. A. M. A.]

DEATH DURING BLOOD TRANSFUSION AS A RESULT OF INTRACRANIAL HEMORRHAGE. J. GLASER, J. EPSTEIN and D. B. LANDAU, Am. J. Dis. Child. **53**:794 (March) 1937.

The authors report a case of intracranial hemorrhage following transfusion in a child of 8 days in whom there had developed uncontrollable hemorrhage after circumcision. The blood of the donor and that of the recipient were compatible. During

the transfusion the child suddenly became cyanotic and died. Autopsy showed an intracranial hemorrhage and bloody cerebrospinal fluid. The posterior fossa was filled with blood. The source of the subtentorial hemorrhage could not be ascertained. Apparently, the brain was not sectioned.

WAGGONER, Ann Arbor, Mich.

CEREBRAL EMBOLISM AS A COMPLICATION OF CORONARY THROMBOSIS. DANIEL L. DIZZI, Am. J. M. Sc. **194**:824 (Dec.) 1937.

Dizzi studied the records of 1,000 consecutive, unselected autopsies from the standpoint of the relationship of cerebral lesions and coronary thrombosis. He found 138 cases of cerebral insults in which the brains were examined at autopsy; in 107 of these there was observed: cerebral hemorrhage, 25; cerebral thrombosis, 77; hemorrhage and thrombosis, 4, and cerebral embolism, 1. In 12 cases (11.2 per cent) there was also coronary thrombosis, which was not diagnosed clinically in a single case and was suspected in only 2. In only 41 of the 1,000 cases was coronary thrombosis established. The indication of a high incidence of unsuspected coronary thrombosis in cases of hemiplegia warrants further study. The heart should be suspected in all cases of cerebral embolism, irrespective of the patient's age.

MICHAELS, Boston.

DISSEMINATED AREAS OF NECROSIS IN THE BRAIN FOLLOWING INTRAVENOUS INJECTION OF NEOARSPHENAMINE. ELINOR R. IVES, Bull. Los Angeles Neurol. Soc. **2**:140 (Sept.) 1937.

Ives reports a case of encephalopathy following administration of neoarsphenamine in which the patient, who did not have syphilis, survived for four months after the drug was given. The histologic changes in the brain may therefore be considered as the ultimate lesions in so-called arsphenamine encephalitis.

A woman aged 38 was given three injections of neoarsphenamine (0.45 Gm.) within a period of seven days in treatment of Vincent's stomatitis. After the fluid injection signs of involvement of the central nervous system developed. The patient died of an ascending urinary infection four months later. Chemical analysis of the brain gave negative results for the presence of arsenic. There was uniform fibrous thickening of the arachnoid membrane. Gross degenerative lesions were present in the thalamus and claustrum on both sides, as well as in the putamen and amygdaloid nucleus on one side. The larger areas were represented by cysts. There were multiple smaller areas of degeneration and scarring in the basal ganglia, the corpus callosum and the subcortical white matter. Some of these areas showed slight glial proliferation, while others consisted of necrosis bordered by fibroblasts and infiltration with round cells and histiocytes. Hyalinized astrocytes and occasional compound granular cells and deposits of pigment were observed at the margin of these areas. The perivascular spaces in the centrum semiovale were markedly dilated and contained pigment-bearing phagocytes. Many blood vessels adjacent to degenerated areas were practically occluded by thickened walls. Perivascular infiltration with round cells was seen in the basal ganglia. Satellitosis and oligodendrogliosis were also present. There was no evidence of hemorrhage, such as occurs in the acute stages of "arsphenamine encephalitis"; all the lesions were quiescent. Ives believes that the lesions in this case were the result of vascular occlusion followed by sclerosis.

MACKAY, Chicago.

CHANGES IN THE BRAIN IN ACCIDENTAL ELECTROCUTION. GEORGE B. HASSIN, J. Nerv. & Ment. Dis. **86**:668 (Dec.) 1937.

Hassin examined the nervous system of a Negro aged 35 years who died of accidental electrocution. The brain was hyperemic and edematous, but otherwise grossly normal. Microscopic examination revealed small cracks or tears in the cerebral tissue, with rarefaction, reticulation or thinning of the parenchyma,

especially around the cracks. The ganglion cells were swollen and showed chromatolysis, or appeared reticular, vacuolated or liquefied and stained poorly. Satellitosis and neuronophagia were present. The cell processes were deeply stained, tumefied and tortuous. These cell changes were present in all layers of the cortex, but were especially marked in the basal ganglia. They were much milder in the medulla oblongata and spinal cord. The axis-cylinders were well preserved. The glia cells were frequently swollen. The smaller blood vessels were surrounded by enlarged spaces of His, while the larger blood vessels exhibited a torn membrana elastica, a change which seemed to be specific to electrocution. The cerebral meninges and subarachnoid space contained many fibroblasts and mesothelial cells, as well as small dark round bodies of the size of a lymphocyte and numerous pigment granules, changes which Hassin states may conveniently be termed aseptic meningitis.

Hassin states that the pathologic changes in the central nervous system are more pronounced in legal than in accidental electrocution, probably because the current is led through the head. Satellitosis and neuronophagia are noteworthy changes because they must take place after signs of death are present. Nerve cells deep in the brain probably die before the glia; hence, neuronophagia occurs. Hassin believes that the essential factor in the cerebral changes accompanying electrocution is a form of "concussion" resulting from the effect of the current on the brain tissues and their blood vessels. Excessive heat generated by the passage of the current through the body is not responsible, since the changes due to hyperpyrexia are different from those resulting from electrocution.

MACKAY, Chicago.

A CASE OF CUSHING'S SYNDROME. C. I. PARHON, S. M. MILCOU and E. TOMORUG, Rev. franç. d'endocrinol. **15**:273 (Aug.) 1937.

This is a clinical and anatomic report of a case of Cushing's syndrome in a man who was first seen at the age of 47. At this time he complained of rapid gain in weight, difficulty in walking, breathing and talking and somnolence. His appetite was ravenous, and he was always thirsty. Examination revealed an obese man, weighing 151.5 Kg., with a heavy layer of fat around the abdomen and pronounced hirsutism in the region of the thorax, back and forearms, especially on the posterior surface. There were ichthyoform changes in the skin in the region of the elbows. Analysis of the blood revealed hyperglycemia and a lowered calcium and cholesterol content. The sella turcica was deep.

Autopsy revealed general macrosplanchnia, the brain weighing 1,908, the liver 2,860, the pancreas 300, the spleen 230, the parotid 100, the right testis 7.5 and the left testis 7 Gm. The hypophysis was enlarged. The anterior lobe showed pronounced disproportion in the distribution of the various types of cells, with new formations of basophilic and eosinophilic cells. There were numerous basophilic adenomas in the anterior and the left lateral part of the lobe. There were also numerous eosinophilic cells in the posterior part of the lobe. These cells showed a reduced protoplasmatic body and a large nucleus. A small number of chromophobe cells were seen in the anterior part and in the periphery of the pituitary gland. The left half of the posterior lobe showed abundant infiltration with basophilic cells.

The thyroid gland showed diffuse hyperplasia. The tissue of the parathyroid gland was formed exclusively of principal cells, with an occasional oxyphilic cell. The adrenal glands were considerably enlarged, the right weighing 17 and the left 11.5 Gm. The cortex of the gland was almost four times as thick as the medulla. The histologic picture of the cortical layer showed unequal distribution of the lipoid substance, which was especially abundant in the deeper parts. The entire architecture was disturbed by the presence of adenomas and islets of spongiocytes. The medullary layer was narrow and infiltrated with cortical cells. The chromaffin cells showed vacuoles which did not give the chromaffin reaction.

NOTKIN, Pougkeepsie, N. Y.

A CASE OF SIMMONDS' SYNDROME. ONARI KIMURA and TAKESI KUROBANE, Psychiat. en neurol. jap. **41**:80 (Nov.) 1937.

Kimura and Kurobane report a case of Simmonds' disease in which autopsy was performed. There were severe marasmus and generalized decrease in size of the organs. In the floor of the third ventricle was a tumor, which filled the third ventricle, destroyed its roof and spread out in the subependymal layer, destroying a large part of the wall of both lateral ventricles and invading the septum pellucidum, the fornix, the pineal gland, the medial part of both thalami and the right caudate nucleus. There was marked internal hydrocephalus. The tumor extended posteriorly through the aqueduct of Sylvius into the fourth ventricle. Extensions were observed in the right cerebellopontile angle and in the right porous acusticus. The hypophysis was normal in size. Microscopically, the anterior lobe showed mild secondary atrophy, while the posterior lobe, infundibulum and floor of the third ventricle were destroyed by tumor. The tumor was a glioma of the glioblastoma multiforme type.

ALPERS, Philadelphia.

A CASE OF PARTIAL ABSENCE OF THE CORPUS CALLOSUM. TETSU HIRESAKI, Psychiat. en neurol. jap. **41**:85 (Nov.) 1937.

Hiresaki reports a case of partial absence of the corpus callosum in a child aged 8 years who died of pulmonary tuberculosis. Examination revealed horizontal and vertical nystagmus, contracture of the lower extremities, inability to stand or walk, rigidity of the entire body, generalized convulsions at times and a Babinski sign bilaterally. The patient was mentally deficient and indifferent to external stimuli. The brain was small and showed partial loss of the corpus callosum, severe decrease in the white matter, with poor development of the centrum semiovale, marked internal hydrocephalus and a small striatum and thalamus. Microscopic study revealed a well developed cortex; cortical layers II, III and V were poor in cells. The corpus callosum was very small and poor in fibers.

ALPERS, Philadelphia.

Psychiatry and Psychopathology

MIRROR BEHAVIOR IN SCHIZOPHRENIC AND NORMAL INDIVIDUALS. SAUL ROSENZWEIG and DAVID SHAKOW, J. Nerv. & Ment. Dis. **86**:166 (Aug.) 1937.

Rosenzweig and Shakow report on an analysis of the behavior of schizophrenic and normal adults in the presence of a mirror. Previous work by others had suggested that such behavior may indicate personality trends and aid in the early diagnosis of dementia praecox. The subjects in the present study were all men and consisted of 10 paranoid and 10 hebephrenic patients and 10 normal persons of comparable age and education. They were provided with toy dolls, furniture and blocks and were asked to construct a scene representing an important event in a child's life. Each subject was left alone to his task in a room closed by a door in which were set three small mirrors of special type, so constructed that they served as ordinary looking glasses to one inside but were transparent to an unseen observer outside the door. The "mirror behavior" of the subjects was classified under four headings: (1) no response; (2) casual response, i. e., momentary, idle notice of the mirror; (3) socially adequate response, such as ordinary use of the mirror for adjusting the necktie or combing the hair, and (4) socially inadequate response, such as autistically motivated mumbling, talking, pantomining, grimacing or self manipulation before the mirror.

The three groups of subjects differed strikingly in their behavior. In general, the normal persons responded casually or socially adequately, 3 of the 10 giving no response at all. Paranoid subjects for the most part appeared unaware of the mirrors, 7 of the 10 giving no response and 3 giving casual or socially adequate responses. The hebephrenic patients, on the other hand, tended to respond pre-

dominantly in either a casual or a socially inadequate fashion. Rosenzweig and Shakow interpret these results as indicating that the normal persons were alert to the environment (casual notice of the mirrors) and socially conscious of the regard of others. The paranoid patient's mirror behavior, on the contrary, indicated that for him outside approval was unnecessary (no response to mirrors) and that other persons in his environment were subordinated to his inner, self-sufficient mental processes. The hebephrenic patient differed from the paranoid patient in being more deteriorated (less control of casual notice of mirrors) and more disorganized psychically, in that "his different partial selves . . . have a kind of intercourse with each other, which absorbs him completely and detaches him from everyday society." In his pantomiming and grimacing before the mirror, the hebephrenic patient treats his image as though it were another person.

MACKAY, Chicago.

THE PSYCHODYNAMICS OF CHRONIC ALCOHOLISM. ROBERT P. KNIGHT, J. Nerv. & Ment. Dis. **86**:538 (Nov.) 1937.

Knight presents a study of the psychodynamics of chronic alcoholism as observed in a selected group of patients in a private sanatorium for nervous disorders. He regards persistent, excessive drinking as a symptom which represents an attempt at solution of a fundamental emotional conflict. Most alcohol addicts exhibit superficial psychologic resemblances, such as glibness, affability and confidence, but the deeper emotional maladjustments responsible for the alcoholism vary widely in different patients. Nevertheless, Knight contends that there must be psychologic principles, common to all patients, which explain precisely why drinking is the chosen method of escape; he outlines a typical case, which was carefully studied, and points out the psychodynamic features which in general are applicable to the whole group.

The mother of the male alcoholic patient has usually been overindulgent and protective; in giving him the breast to satisfy his infantile distresses, in vacillation in weaning or in poor handling of thumb sucking, she fosters the development of oral-erotic patterns, or the desire to take something into the mouth for comfort and relief. At the same time, by her overindulgence of the child, her intercession in his behalf with a stern father and her exaggerated protection she stimulates in the child an excessive desire for the personal affection and indulgence of all his companions and associates. Such demands are doomed to frustration in the world of adults, and to this frustration he reacts with intolerable disappointment and rage. At this stage the solace of oral gratfication is sought in alcohol, while his reactions of rage lead to hostile acts and wishes against those who have failed to supply the desired personal affection and indulgence. Such hostile wishes lead to guilt and masochistic tendencies, and hence to further excessive need for "affection and indulgence as proof of affection." These excessive claims on others, being doomed again to frustration, lead in turn to further disappointment and rage, and a vicious circle is thus completed. The use of alcohol as solace for such depressing emotions is determined by the early patterns for oral gratification set up through the mother's pampering. Later, alcohol leads to destruction of esthetic values and self respect, and thereafter it serves further to satisfy the masochistic and self-punishing needs produced by the sense of guilt.

MACKAY, Chicago.

PERSONALITY STUDIES IN ALCOHOLIC WOMEN. FRANK J. CURRAN, J. Nerv. & Ment. Dis. **86**:645 (Dec.) 1937.

The problem of alcoholism in women has received scant attention. Curran studied the sociologic and psychologic characteristics of 50 alcoholic women. Of the 50, 34 were psychotic; these 34 subjects and 31 other alcoholic patients with psychoses were studied as regards the nature and content of the hallucinoses. The two largest groups encountered were those with acute hallucinosis and delirium tremens. All the patients were of low economic status; Irish and Negro

women formed the largest racial groups; the ages varied from 17 to 63 and averaged 39.86. Forty-three of the original 50 women had been married; of these 22 were widowed, divorced or separated from their husbands. Three of the 7 unmarried women had common law husbands; 1 was a prostitute, and the remaining 3 had solitary sex experiences. The majority were shy, reserved and emotionally unstable and showed marked attachment to the mother. Forty-four of the 50 women denied autoerotic, and 48 homosexual, practices. Forty-six denied all perversions. Only 20 had satisfaction in heterosexual life. Sixteen had always been frigid and 5 others had infrequent orgasms. Drinking habits were solitary in 34 patients, but most of the women said they drank to increase their sociability and so lessen their emotional tensions. Somatic findings included: unequal, irregular or sluggish pupils in 14 patients, convulsions in 5, and a positive Wassermann reaction of the blood in 2. For the 2 patients last mentioned the findings in the spinal fluid were normal. None presented evidences of gonorrhea.

Through a study of the content of the hallucinations experienced by these women Curran found much to confirm the trends already suggested in the sociologic and personality studies. The predominance of sexual, chiefly heterosexual, problems, as well as marked narcissistic interest in the body, was evident in the hallucinations. These patients particularly feared removal of the receptive sex organs, as well as mutilation of the rest of the body. The voices accused the patients chiefly of prostitution, homosexuality, degeneracy, perversions, masturbation and incest. Over half the patients recognized the identity of the person speaking in the hallucinations.

From these studies, Curran believes that "the woman who later becomes a chronic alcoholic has been hindered in her heterosexual adaptation at an early age, and has, therefore, to go back to more primitive sexual tendencies of oral, anal and narcissistic character." The alcoholic woman is socially inadequate, has little interest in men and is often frigid. Contrary to public opinion, she does not express her heterosexuality more freely in acute alcoholic intoxication. She strives for social recognition and fears this will not be achieved. Overt homosexuality is rare among alcoholic women, but many have great interest in their own bodies and those of other women. These traits seem to have resulted from special attachment to the mother and severe repression of the sexual functions. There are, thus, marked narcissism, fear of sexual and general somatic mutilation and, consequently, strong aggressive tendencies, as manifested during intoxication and in the hallucinoses.

MACKAY, Chicago.

MARITAL HAPPINESS IN TWO GENERATIONS. PAUL POPENOE and DONNA WICKE, Ment. Hyg. **21**:218 (April) 1937.

About half of the unhappily married persons who consulted the Los Angeles Institute of Family Relations had family backgrounds which were themselves unhappy. On the other hand, in a group of apparently happily married couples used as controls, only from 15 to 18 per cent came from unhappy parental homes. That being brought up in a happy family has some influence on the ability to live happily in a subsequent marital relationship is a reasonable inference. Popenoe and Wicke, however, are unwilling to state to what extent this represents a hereditary biologic adequacy and to what extent it is due to the effect on children of a wholesome cultural pattern. They advance the safe conclusion that marital unhappiness in many instances is due to the interacting influence of bad heredity and bad environment.

DAVIDSON, Newark, N. J.

CONVALESCENCE. EDWARD LISS, Ment. Hyg. **21**:619 (Oct.) 1937.

Illness of prolonged duration or great intensity brings in its wake a need not only for physical recuperation but for emotional readjustment. The more prolonged or the more traumatic the illness the more likely it is that the organism

will regress to early infantile, or essentially physical, concerns. The age of the patient is important, and regression to the early stages of development is much more probable in the immature than in the mature. More recently acquired habits or cultural patterns are the first to go. The physician and the nurse easily fall into the role of parent substitutes for the patient. In this situation fear in the form of a primitive reflex may develop and be transformed by insight and repression into constructive activity. There may also be (*a*) pathologic repression with latent anxiety in the form of symptoms of hypochondriasis or (*b*) flight into a neurosis involving the various manifestations of the psychobiologic self, referred to as hysterical symptoms.

The individual response to illness (a trauma) is paradoxic. The initial reaction is one of anxiety, conscious or unconscious, followed by the syndrome pattern particular to the individual patient. This pattern often masks and blankets the actual pathologic condition. The organism may respond to a loss in three major ways, or there may be a combination of responses. In certain persons a loss may be an incitement to compensation, so that the patient may emerge from the illness with greater maturity. Another group, overwhelmed by the loss, reverts to the pattern of physical symptomatology. In illness, whether acute or chronic, reeducation into reality is a vital part of convalescence as a bridge to life when it begins outside the institutional walls. Illness beyond a certain duration entails emphasis on educational technic as much as on purely physical details of therapy, and a vital part of any program for the handling of the chronically ill, whether adults or children, should be a school for reeducation.

CORSON, Stockbridge, Mass.

PAGET'S DISEASE, WITH MENTAL SYMPTOMS AND CHOROIDITIS. J. L. CLEGG, Lancet **2**:128 (July 17) 1937.

Clegg reports the case of a man aged 64 who was admitted to the hospital because of acute confusion, restlessness, auditory and visual hallucinations and irrelevant speech. There were the usual findings of Paget's disease, namely deformity of the skull, chest and long bones; in addition, there was "severe retinal degeneration with fibrinous exudate, somewhat resembling the senile type of choroidoretinal degeneration." The patient, however, recovered from the mental confusion, with no residual dementia, and was adjudged normal mentally. He died of an attack of acute heart failure; necropsy revealed no noteworthy changes.

Clegg refers to 13 additional cases in the literature in which mental symptoms were pronounced, although Paget in his original description stated that osteitis deformans is not associated with mental changes. Hahn reported the case of a woman aged 63 whose mental picture was one of "gradual mental deterioration with loss of initiative and emotional apathy." This condition was accompanied by epileptic seizures. Stander, in 2 cases, reported impairment of judgment and loss of memory, with periods of confusion, visual hallucinations and sensory aphasia. Schrijver noted in 4 cases of Paget's disease a mental picture which was essentially a delusional psychosis accompanied by auditory hallucinations; an occasional epileptiform seizure occurred, and the behavior suggested schizophrenia. Another of his patients showed a syndrome which resembled Korsakoff's psychosis; still another showed emotional instability, forgetfulness, depression and paranoid delusions. Subsequently, this patient had a cerebral accident, and a parkinsonian picture developed. In the other cases reported in the literature the mental symptoms varied considerably. In some the mental aberrations came after the changes in the bones; in others there did not seem to be any intimate relationship between the two. In a case reported by Kaufman Paget's disease was associated with a cerebral tumor, which was discovered at autopsy. Depression and hypochondriacal or suicidal tendencies occurred. The mental picture associated with Paget's disease was similar to that of the involutional or senile psychoses. This, Clegg believes, lends support to the idea that the mental symptoms associated with Paget's disease are the result of cerebral arteriosclerosis.

KRINSKY, Boston.

VASOMOTOR REACTIONS AND HEAT REGULATIONS IN CATATONIC STUPORS. R. JUNG and E. ARNOLD CARMICHAEL, Arch. f. Psychiat. **107**:300 (Nov.) 1937.

The activity of the sympathetic nervous system and heat regulation were studied in 8 cases of akinetic catatonia. The investigation was carried out by finger plethysmograms, thermoelectric registration of the cutaneous and rectal temperatures and observation of reactions to warming and cooling of the body. These results were compared with observations on a large group serving as a control which consisted of 50 normal persons and 200 patients suffering from other types of diseases. Associated with catatonic stupor the authors found a tendency to peripheral vasoconstriction and coldness of the extremities at medium or low external temperatures. With these reactions there were combined, in most cases, pronounced cyanosis and some edema of the extremities. Similarly, vasodilatation following an increase in the temperature took place at a slower rate in these patients than in the material used as a control. It was found, however, that all these deviations could be explained on the basis of the decreased mobility of these patients and could be reproduced in healthy persons when they were placed under the same conditions. No disturbances could be discovered in the vasomotor control or the heat regulation of patients with catatonic stupor. The cutaneous vessels of catatonic patients when in a state of dilatation were found to react to various external and internal stimuli, including injections of small doses of epinephrine, in a manner similar to that in normal persons. The authors state that their studies show that there is no reason to assume any characteristic disturbance in the function of the central or the peripheral vegetative nervous system in akinetic catatonia.

MALAMUD, Iowa City.

Meninges and Blood Vessels

EXPERIMENTAL MENINGITIS IN GUINEA-PIGS. SARA E. BRANHAM, R. D. LILLIE and ANNA M. PABST, Pub. Health Rep. **52**:1135 (Aug. 20) 1937.

Continuation of study of the effects of injections of meningococci and meningococcus products into the cisterna magna of guinea pigs is reported by Branham and her collaborators. Their earlier experiments were reported in 1932. Young guinea pigs, weighing from 200 to 250 Gm., were inoculated intracisternally, under ether anesthesia, with living cultures of meningococci, with heat-killed cultures, with filtered suspensions of living cultures and with broth filtrates. The weight and temperature were recorded daily for each animal as long as it was under observation. The cultures were of freshly isolated strains. The dose given to guinea pigs usually varied between 10,000,000 and 100,000,000 meningococci, depending on the virulence of the strain. The number of meningococci injected was contained in a volume of from 0.2 to 0.3 cc. of Ringer's solution. Purulent meningitis was produced alike by living meningococci, by killed cultures, by Berkefeld filtrates of suspensions from agar cultures (suspension filtrates) and by filtrates of broth cultures. The meningeal exudate appeared in from three to five hours. It was predominantly purulent, was densest on the base of the brain and between the brain stem and the occipital cortex and was often accompanied by congestion and hemorrhage. Fibrin was most often evident after inoculation with killed cocci. The sheaths of perforating and, less often, deep vessels were often infiltrated with purulent exudate. Purulent thrombosis was not infrequent, being especially common after inoculation with killed cocci. Purulent exudate in the ventricles occurred in the majority of the animals inoculated with living or killed cultures and in about 75 per cent of those receiving broth filtrates and dying in less than thirty hours, but it was infrequent with the suspension filtrates. Infiltration of the choroid plexuses was correspondingly frequent. Purulent infiltration of the brain substance abutting on the meninges or ventricles was observed in more than 50 per cent of the animals inoculated with cultures or broth filtrates. Other less frequent features of the process were perivascular hemorrhages, miliary marginal

or central abscesses and suppurating ependymal ulcers in the ventricles. Pericellular edema in the cerebral cortex and tigrolysis and vacuolation in the nuclei of the brain stem were observed frequently, especially in animals surviving more than twelve hours. In subsiding reactions the meningeal exudate decreased in amount and became partly or entirely lymphocytic; the involvement of intracerebral vascular sheaths disappeared, and the ventricular exudates decreased and disappeared. Plexal infiltration became lymphocytic or disappeared. With filtrates and killed cultures evidence of subsidence was observed on the second day, while with living cultures no decrease in the reaction was apparent until after three days. It appears that meningococcic meningitis in guinea pigs may be either an infection or an intoxication. In both infection and intoxication the clinical and histopathologic pictures were the same.

EDITOR'S ABSTRACT.

ACROCYANOSIS. EDWARD SAMUEL STERN, J. Ment. Sc. **83**:408 (July) 1937.

When normal skin is moderately cold it becomes blue, owing to contraction of the arteries and arterioles and to relaxation of the capillaries and the subpapillary venous plexus of the epidermis. When the blue color is deep, the condition is called acrocyanosis. The disturbance, although rare in the general population, is common among patients in hospitals for mental disease. Stern differentiates this condition from thrombo-angiitis obliterans and Raynaud's disease. Acrocyanosis occurs with striking frequency in cases of catatonic dementia praecox.

Fifty-five patients of each sex were studied and were examined again four years later. Acrocyanosis was two and one-half times as common in persons who are inactive and allow themselves to be chilled as in those who are normally active. There was no evidence of endocrine dysfunction in these cases. Lewis' test of immersion of the hands in cold water was used to test the elasticity of the arteriolar and venous systems. Histologic examinations were made of the distal portions of the extremities.

Stern concludes that acrocyanosis is a true clinical entity. It may affect the hands or feet or both. It causes little disability. It is due to moderate cooling of the affected parts in conjunction with chilling of the body as a whole. Age and sex have no special influence on the incidence. The mechanism of acrocyanosis consists in partial obstruction to the arterial blood supply of the skin of the affected parts. There is no evidence of venous obstruction. The arterial obstruction is due to an increase in the muscle layer of the media of the arterioles and not merely to arteriolar spasm. There is no evidence of pathologic changes in the blood, nervous system or endocrine glands. In severe forms recovery from the attack may occur only after days of warmth.

KASANIN, Chicago.

TUBERCULOSIS OF THE CENTRAL NERVOUS SYSTEM, WITH ESPECIAL REFERENCE TO TUBERCULOUS MENINGITIS. A. R. MACGREGOR and C. A. GREEN, J. Path. & Bact. **45**:613 (Nov.) 1937.

Macgregor and Green declare that the ideal method for the isolation of tubercle bacilli from the cerebrospinal fluid is the utilization of both direct culture and inoculation of guinea pigs. If direct culture is adopted, the Löwenstein-Jensen medium is likely to be of more service than the mediums used more commonly as a routine. Of a series of eighty cases of tuberculous meningitis, the infecting organism was of the human type in 76 per cent and of the bovine type in 24 per cent. Of these cases 2 per cent occurred in the first six months of life, 14 per cent in the first year and 81 per cent within the first decade. The human type of organism was responsible for 91 per cent of cases of primary thoracic infection terminating in tuberculous meningitis, and the bovine type, for 9 per cent. By contrast, the two types were responsible for approximately equal numbers of cases in which the disease terminated in meningitis with an initial focus of infection in the abdomen. It was reasonably certain that the exudative meningitis had arisen

from a localized lesion. In one case the lesion responsible was in the spine; in the others it was in the brain or meninges. The localized lesions in the central nervous system took the form of caseous nodules in the substance of the brain and cord, tubercles or deposits of tuberculous exudate in the meninges or choroid plexus and areas of tuberculous meningo-encephalitis. In twenty-five cases of tuberculosis without meningitis examination was made for evidence of infection of the central nervous system. In eleven of twenty-four cases localized tuberculous lesions were observed in the brain. In ten of twenty specimens of cerebrospinal fluid tubercle bacilli were demonstrated. In forty-five cases in which there were symptoms of cerebral or meningeal irritation and a reaction to the tuberculin test, the cerebrospinal fluid was examined for tubercle bacilli and other evidence of tuberculous infection. In three cases tubercle bacilli were isolated, and in two others the cerebrospinal fluid showed cytologic changes strongly suggestive of tuberculous infection. In no case did fatal tuberculous meningitis develop.

EDITOR'S ABSTRACT.

STATISTICS ON ETIOLOGY OF TUBERCULOUS MENINGITIS. P. NOBÉCOURT and S. B. BRISKAS, Presse méd. **45**:1131 (Aug. 4) 1937.

The statistics presented by Nobécourt and Briskas cover the fifteen years from 1921 to 1935, inclusive, and concern children up to the age of 15. In 13,331 hospitalized patients 344 cases of tuberculous meningitis were discovered. The disease does not occur in infants who have not completed the third month of life, and it is rare between the ages of 3 and 12 months (1.2 per cent of the general morbidity). It becomes slightly more frequent between the ages of 12 and 18 months (2 per cent), but after that it increases, reaching 5.2 per cent of the general morbidity in children of 3, 4, 5 and 6 years of age. It is most frequent during the fifth year of life, in that it attains a frequency of 6.2 per cent of the general morbidity. The incidence decreases again from the sixth year on, amounting to 3.5 per cent of the general morbidity in children from 7 to 10 years of age and 2.2 per cent in those from 11 to 15 years of age. It is about the same in boys and in girls, but during the second year it is twice as frequent in girls. As to seasonal fluctuations, the maximum is reached in March and the minimum in October. It is more frequent during the summer months (from April to September) than during the winter months (from October to March). The incidence of tuberculous meningitis has slightly decreased in recent years. This diminution seems to be connected with the decreased incidence of tuberculosis in general. As compared with other tuberculous disorders, tuberculous meningitis is relatively infrequent in children less than 18 months old (approximately 25 per cent of all forms). It increases to 53 per cent during the fifth year of life and subsides to 18 per cent. The source of the infection is unknown in the majority of cases of tuberculous meningitis.

EDITOR'S ABSTRACT.

CLINICAL ASPECTS OF TUBERCULOUS MENINGITIS. L. SCHLAPOBERSKY, Jahrb. f. Kinderh. **149**:215 (July) 1937.

Schlapobersky reports observations on 60 patients with tuberculous meningitis who came for observation at the university clinic in Berne, Switzerland, and also cites reports from the literature. He found that tuberculous meningitis does not present a uniform clinical picture but may appear in many forms. On the basis of the symptomatology, he differentiates seven forms: the classic type, the gastrointestinal type, the narcoleptic type, the convulsive (chiefly tonoclonic) type, the hemiplegic type, the latent type and the type in which consciousness is not impaired. Occasionally there are combinations of various types. The temperature varies in different cases of tuberculous meningitis. The tuberculin reaction is usually positive (79 per cent of the author's cases). The changes in the cerebrospinal fluid vary. Increased pressure is frequent. Tubercle bacilli were discovered in 31.7 per cent of the author's cases. Other changes occurring with considerable

frequency were positive reactions to the Pandy and Nonne-Apelt tests, reduction in the sugar content and increase in the number of cells. The sedimentation speed was nearly always reduced. In 54 per cent of the cases it was possible to demonstrate the source of infection.

EDITOR'S ABSTRACT.

TUBERCULOUS PACHYMENINGITIS. O. KOCH, Ztschr. f. Tuberk. **78**:318 (Sept.) 1937.

Koch cites reports from the literature which indicate that tuberculous pachymeningitis is a process accompanying tuberculosis of adjoining organs and that it develops by contact. However, he observed still other forms of pachymeningitis. In this paper he gives attention chiefly to the relations between tuberculous leptomeningitis and tuberculosis of the brain, on the one hand, and tuberculous inflammation of the dura, on the other. There is reason to assume that tuberculosis of the pachymeninx may develop after that of the leptomeninges, simultaneously with it or even before. There is, in other words, an independent, hematogenically metastasizing tuberculous process of the dura mater. The author differentiates three types: 1. Internal tuberculous pachymeningitis, which develops by contact infection. The most frequent form of this type, the fine nodules that accompany tuberculous leptomeningitis, has been described before, particularly by Huebschmann, who emphasized that this form of nodular tuberculosis of the dura is not seen in all cases of tuberculous leptomeningitis. It is often absent in cases of recent tuberculous basal meningitis. It is difficult to say in what stage of development the leptomeningitis must be in order to produce infection of the dura. 2. Tuberculous pachymeningitis in which the dependence on tuberculous processes in the leptomeninges is possible but not proved. Koch reports 3 cases. In 2 there existed, in addition to the changes in the dura, numerous solitary tubercles of the brain; in the third case they were absent. 3. Independent hematogenic metastasis. In one case the brain could be lifted from the two large tubercles of the dura without loss of substance. The corresponding portions of the brain showed depressions that were entirely smooth and were still covered with pia mater. Thus, it cannot be said that the tuberculomas had been torn from the brain and only adhered to the dura. There also existed a tubercle in the substance of the brain, but this was nowhere in contact with the surface, so that it could not give rise to an infection of the dura and the leptomeninges. Koch regards tuberculomas of the dura as independent hematogenic metastases caused by the same dissemination as the tubercle in the brain itself. He cites a case in which there existed a tubercle only of the dura, all other parts of the brain being free from tuberculosis. Finally, he describes a form of tuberculosis of the meninges that developed in the course of primary tuberculosis in a child. In this case microscopic examination disclosed extensive changes in all layers of the dura and also in the leptomeninges.

EDITOR'S ABSTRACT.

MENINGISM IN LEUKEMIA AND IN WEIL'S DISEASE. J. E. MINKENHOF, Nederl. tijdschr. v. geneesk. **81**:4448 (Sept. 18) 1937.

Minkenhof reports several cases in which there were symptoms of severe meningism. The first patient had subacute lymphatic leukemia which presented the aspects of meningococcic sepsis with meningitis. Minkenhof points out that neurologic changes are occasionally observed in patients with leukemia, and he reviews the literature on neurologic changes associated with leukemias. The other patients had Weil's disease. In these patients the only symptoms were pyrexia and meningeal irritation. The author shows that in patients with Weil's disease the degree of meningism, the composition of the cerebrospinal fluid and the possible occurrence of Leptospira in the arachnoid space show no direct relationship. Several other authors have made the same observation; namely, that in all forms of Weil's disease the spinal fluid may be normal as well as abnormal. Apparently, it is often possible to detect Leptospira in the spinal fluid during the first week of

Weil's disease. Minkenhof emphasizes that in all cases of meningism and serous meningitis in which the cause is obscure the possibility of infection with Leptospira should be taken into consideration. EDITOR'S ABSTRACT.

Diseases of the Brain

TRAUMATIC DIABETES INSIPIDUS. CARL W. RAND and GEORGE H. PATTERSON, Bull. Los Angeles Neurol. Soc. **2**:163 (Dec.) 1937.

Diabetes insipidus is uncommon after injuries to the head. Rand and Patterson report 6 cases occurring in private practice. All the patients were males, of ages varying from 10 to 24 years. Two were injured in automobile accidents, and 2, by falls; 1 was kicked by a horse, and 1 was struck by a falling rock. The injury to the head was severe in all cases, being followed by unconsciousness lasting in some cases for several days. Fracture of the base of the skull was established by clinical or roentgen examinations in 4 cases and was considered probable in the other 2. The intake of fluid varied from 4 to 9 liters, with a correspondingly elevated output of urine. Often, the increase in water exchange was delayed in onset by the fact that the patient remained unconscious for days, and hence could not demand fluids. This delay amounted to ten and fourteen days in 2 cases. Elevation of the blood sugar was not observed, and glycosuria did not occur in any case. One patient showed sharp bitemporal hemianopia which was thought to be due to anteroposterior splitting of the chiasm. Another had a subdural hematoma over the right temporal region, which was removed surgically. A third patient had cerebrospinal rhinorrhea and a subsequent abscess of the right frontal lobe, for which operation was performed. This patient had generalized convulsive seizures. Solution of posterior pituitary was used in 3 of the 6 cases, with reduction in the urinary output. Complete recovery occurred in 4 of the 6 cases, in only 2 of which solution of posterior pituitary was given. The recovery, apparently uninfluenced by this medication, required from three to six months. Partial recovery was observed in 2 cases for two and eight months, respectively. Other common sequelae of injury to the head, such as headache and dizziness, were also observed in several cases. The diabetes insipidus was attributed to injury to the infundibular region of the brain.

MACKAY, Chicago.

TONIC PUPILS WITH ABSENT TENDON REFLEXES: THE SO-CALLED HOLMES-ADIE SYNDROME. KARL O. VON HAGEN, Bull. Los Angeles Neurol. Soc. **2**:171 (Dec.) 1937.

In 1931 Gordon Holmes found 54 cases of tonic pupils reported in the literature, in 19 of which there was also loss or diminution of the tendon reflexes, an association which had first been noted in 1906 by Marcus. Adie reported 5 cases of tonic pupils with absence of tendon reflexes in 1931 and 8 cases in 1932. He stated that the complete form of the disorder includes both the tonic pupils and the absence of one or more tendon reflexes, but that incomplete forms occur in which either the pupillary changes or the disturbances in the tendon reflexes may be absent or atypical. The name "Holmes-Adie syndrome" was proposed by Bramwell in 1936.

The "tonic pupil" does not react to light when tested by the usual bedside methods, but slowly dilates in an hour or so in complete darkness. When placed in bright daylight it slowly constricts to a size smaller than before dilatation, after which it enlarges to its original size. In convergence such a pupil contracts with increasing slowness through a greater range than normal, sometimes attaining the size of a pinhead. When convergence is relaxed pupillary dilatation is delayed and proceeds more slowly than did constriction, the pupil reaching normal size only after many seconds or minutes. Subjectively, the patient notices a similar

sluggishness of accommodation for near or far objects. There may be headache from reading or sensitivity to bright light, but in many cases the patient is unaware of any pupillary disturbance.

The condition usually develops rapidly and then remains stationary, but improvement or progression may occur. About 80 per cent of the cases occur in females, and in 80 per cent of the cases the condition is monocular. The affected pupil is usually the larger; it dilates promptly to a mydriatic drug and constricts with physostigmine. The etiology of the disease is not known. Holmes expressed the belief that a lesion of the third nerve or of its nuclear connections is responsible and that when tendon reflexes are reduced there is also disease of the gray matter of the brain stem and spinal cord.

Von Hagen reports 2 cases, both occurring in women, one of whom was 32 and the other 27. In the first case the right pupil was 4.5 and the left 1.5 mm. in diameter; both reacted slowly, but completely, to light. The right pupil also reacted slowly in accommodation; the left, promptly. Reflexes in the upper extremities were normal; those in the lower extremities, especially the ankle jerks, were greatly reduced. The Wassermann reactions of both the blood and the spinal fluid were negative. In the second case the pupils were both 4 mm. in diameter and irregular; they reacted sluggishly to light, but promptly in convergence. They required thirty seconds to return to their normal size after relaxation. All the tendon reflexes were absent. There were no other evidences of syphilis, but no studies of the blood or cerebrospinal fluid were reported.

MACKAY, Chicago.

CEREBRAL THROMBOSIS CAUSING DELETION OF ARTIFICIAL WRITING CENTER IN LEFT CEREBRAL HEMISPHERE OF LEFT-HANDED MAN. J. M. NIELSEN, Bull. Los Angeles Neurol. Soc. **2**:176 (Dec.) 1937.

Nielsen reports the case of a man who was "born left handed," was forced to write exclusively with his right hand in school and had never written with the left hand since the age of 8 years. At the age of 68, while suffering from severe arterial hypertension and arteriosclerosis, he had left hemiplegia with complete motor and sensory aphasia. The aphasia lasted twenty-four hours, and the hemiplegia, three weeks. Seven months later he awoke with right hemiplegia, which left the right hand sufficiently free for attempts at writing. He then had agraphia with the right hand, being unable to write a single letter with that hand, though he could write numbers to dictation. Ability to write with the left hand was preserved, but he could not copy with the right hand what he had written with the left. He could read without difficulty, cut with scissors held in the left hand and draw pictures with either hand. Mental calculation was impaired. Three days later the hemiplegia had greatly diminished, but it was not until the twelfth day that he could again write with the right hand.

Nielsen believes that the patient had two "writing centers," one on each side of the brain, but that the center for general knowledge of language remained in the right hemisphere, with connections between the two centers through the corpus callosum. Recovery from the aphasia associated with the first (left) hemiplegia could not have been due to substitution of the left center for the right but must have resulted from restoration of the function of the right center, since the subsequent right hemiplegia produced only agraphia, not total aphasia. The "writing center" in the left hemisphere was "artificial," and at the time of the second, or right, hemiplegia, it was separated by the lesion from the language area on the right side of the brain.

MACKAY, Chicago.

FRACTURE OF SKULL INVOLVING PARANASAL SINUSES AND MASTOIDS. C. C. COLEMAN, J. A. M. A. **109**:1613 (Nov. 13) 1937.

Coleman points out that fractures of the skull, whether of the vault or base or, as they usually are, of the two in combination, frequently produce serious damage to the brain and that the cerebral injury should receive primary con-

sideration. Fracture involving a paranasal sinus is often only a minor effect of an injury which damages important regions of the brain at the base of the skull and severely lacerates the cerebral cortex by the indriven fragments of an associated compound fracture of the vault. Consideration of the sinal fracture in cases of serious trauma to the head must at times be postponed, or even abandoned, in favor of a management which gives the patient the best chance to withstand the primary effects of his injury. The two main objectives of surgical treatment of trauma to the head are the prevention of infection and the removal of intracranial hematomas. The dangers of fracture involving the paranasal sinuses depend almost entirely on the laceration of the dural covering, and the only positive sign of such laceration is leak of cerebrospinal fluid or pneumocephalus. Cerebrospinal fluid leaks may result from fracture involving any of the cranial sinuses. In a series of 940 cases of trauma to the head there were 216 fractures of the skull, with 87 fractures of the base. Of the 87 basal fractures, 15 involved the frontal sinuses; 6 of these were associated with severe depressed compound fracture of the frontal vault, and operation was promptly done for disinfection, débridement and closure of the dura. One patient with a slightly depressed compound fracture of the outer wall of the frontal sinus was treated by debridement and suture of the laceration overlying the fracture. Prompt recovery followed in this group. In all cases of linear fracture involving the frontal sinus there was prompt recovery without operation. In another case the patient died of meningitis eleven days after admission. In addition to the fracture of the right frontal sinus, autopsy disclosed comminution of the ethmoids, with extension of the fracture through the petrous portion of the temporal bone on the right side. Extensive laceration of the brain was present, and fractures of both arms, thigh and ribs and an injury to the chest indicated the body-wide violence of the trauma. This case illustrates the difficult situation not infrequently found in dealing with fracture of the skull involving the paranasal sinuses. In a few cases the author has exposed the anterior ethmoid sinuses to close a laceration in the dura when there was a persistent leak of cerebrospinal fluid. The dangers of coughing, sneezing and straining when there is a basal fracture have been frequently emphasized. Vomiting and respiratory difficulties of the unconscious patient also increase the risk of intracranial infection in the early stages of the injury, and meningitis often develops in the first few days. Pneumocephalus is a rare complication of trauma to the head. In cases of acute injury to the head, the discovery of intradural air should lead to repeated roentgen examinations to determine whether the amount of air is increasing or diminishing. If it is increasing or is stationary for three or four days and cerebrospinal fluid is escaping, surgical intervention for closure of the dural laceration is indicated. Fractures of the mastoid and petrous portion of the temporal bone are recognized usually by such indirect evidence as bleeding from the ear in the absence of injury to the external canal, escape of cerebrospinal fluid, Battle's sign and involvement of the seventh and eighth nerves. Hemorrhage from the ear is rarely profuse, and no treatment is required except cleansing the external canal and auricle with alcohol and covering the ear with a sterile dressing. There is not infrequently a collection of blood in the middle ear, and this may become infected, giving rise to otitis media and mastoiditis. Early surgical treatment of mastoiditis secondary to fracture is of the greatest importance. It is obvious that the welfare of the patient with fracture of the mastoid or the petrous portion of the temporal bone is best protected when there is close cooperation between the otologist and the neurologic surgeon. In 49 of the 87 cases of fracture of the base of the skull there was free bleeding from one or both ears. Four patients died as a result of intracranial infection, giving a mortality rate of 8.16 per cent. In 2 cases disabling Ménière's syndrome followed fracture of the petrous portion of the temporal bone. In these cases there were deafness, leak of cerebrospinal fluid after injury and temporary facial paralysis. Intracranial section of the auditory nerve completely relieved 1 patient, while the other did not improve but refused operation.

EDITOR'S ABSTRACT.

MALIGNANT TUMORS OF THE NASOPHARYNX, WITH SPECIAL REFERENCE TO THE NEUROLOGICAL COMPLICATIONS. WILLIAM NEEDLES, J. Nerv. & Ment. Dis. **86**:373 (Oct.) 1937.

Malignant tumors of the nasopharynx are relatively rare. They tend to invade the base of the skull and to produce neurologic symptoms while remaining silent at their site of origin. Needles contributes a clinical study of 35 cases of such tumors, 25 of which occurred in males and 10 in females. The tumors were most commonly observed in the fifth and sixth decades of life. In 19 of the 35 cases there were no neurologic manifestations; even in these, local pharyngeal disturbances were often absent. In such cases the presence of pathologic cervical lymph nodes often furnished the clue to the diagnosis. In 16 of the 35 cases there was involvement of one or more cranial nerves. This represents a somewhat greater incidence (45.7 per cent) of neurologic complications than is usual with malignant tumors of the nasopharynx. In 3 cases neurologic complications, such as sensory disturbances over one side of the face, oculomotor impairment and ptosis and diplopia, were the first evidences of a nasopharyngeal tumor. The cranial nerves most frequently involved were the trigeminal and abducens, the trigeminal nerve being affected in 10 cases and the abducens in 14. Disturbances of the sensory root of the trigeminal nerve were manifested by pain, paresthesias and hypesthesias. The oculomotor and trochlear nerves were the next most frequently involved, one or both being affected in 8 cases. The lower cranial nerves were less frequently implicated, and the olfactory and optic nerves were rarely involved. The auditory nerve was not affected in any case, but symptoms referable to the ear, such as tinnitus, pain or conduction deafness, were frequent and seemed to be due to obstruction of the eustachian tube by the tumor. The pyramidal tracts were involved in only 1 case, while Horner's syndrome occurred in 4 instances, either from disturbance of the sympathetic fibers coursing with the ophthalmic branch of the trigeminal nerve or from pressure of lymph nodes on the cervical portion of the sympathetic trunk. Papilledema occurred only twice.

Needles emphasizes the importance of examination of the nasopharynx on the slightest suspicion of malignant tumor if the diagnosis is not to be missed. Roentgenologic examination was of aid in 14 of the 16 cases, chiefly in demonstrating rarefaction of bone at the base of the skull, thinning of the sella turcica or erosion of the wall of a sinus or orbit. The average duration of the illness in the series was twenty-eight months. Treatment of the nasopharyngeal tumor with radium appeared to mitigate the symptoms and to prolong life, but the results were far from satisfactory. Earlier diagnosis and treatment offer some promise of improving the therapeutic results.

MACKAY, Chicago.

CYSTOMETRIC OBSERVATIONS IN ASYMPTOMATIC NEUROSYPHILIS. E. L. BRODIE and I. A. PHIFER, J. Urol. **38**:412 (Oct.) 1937.

In an effort to determine whether in proved cases of asymptomatic neurosyphilis there is any preclinical evidence of neurogenic bladder before frank symptoms appear, Brodie and Phifer studied 24 unselected cases of asymptomatic syphilis of the central nervous system. Positive serodiagnostic tests of the spinal fluid were obtained in all cases; in none was there urinary infection. There were 16 men and 8 women, from 25 to 59 years of age. The initial lesion was known in all but 12 cases. The duration of the disease was unknown in any of the women studied. No correlation of the initial lesion, the duration of treatment and the cystometric observations could be drawn. In the cases in which cystometry was employed, the bladders were compensated, as evidenced by the absence of residual urine and freedom from urinary symptoms and infections. In 4 cases the cystometrograms were normal; in 4, while the findings were apparently within normal limits, there were a latent desire to void and signs at least suggestive of early neurogenic involvement, and in 16 there was a preclinical neurogenic bladder, according to the usual criteria for interpretation. Cystoscopy was performed in

17 cases, in 4 of which there was a neurogenic bladder. In 5 cases the observations, while suggestive, were alone insufficient for a definite diagnosis. In 3 cases cystoscopy apparently revealed nothing abnormal, while the cystometrograms demonstrated neurogenic bladders.

EDITOR'S ABSTRACT.

EPILEPSY OF ALLERGIC ORIGIN. N. W. CLEIN, Northwest Med. **36**:378 (Nov.) 1937.

Clein discusses forms of epilepsy which should be subjected to a painstaking allergic study. The particular criteria necessary to make a diagnosis of allergy, regardless of the symptoms, are: 1. A positive family history of allergy, which is present in practically every case. 2. Previous allergy in the same person, such as eczema, pylorospasm or certain types of gastrointestinal distress in infancy and, later, urticaria, hay fever, asthma, "chronic nose catarrh" or "sinus trouble," migrain, canker sores, mucous colitis and vague gastrointestinal complaints. 3. Presence of active allergy, manifested chiefly by recurrent, frequent colds and a chronic cough. When it has been determined that the history of the patient and his family at least suggests an allergic background, thorough study, including cutaneous and intradermal tests, is indicated. This is particularly desirable in cases in which improvement has not been shown with treatment for epilepsy. The treatment may require simple elimination of allergic foods, a "dust-free" environment, desensitization with a specific antigen or a combination of all these methods. This type of treatment can hope to be effective only in cases in which there is conformity to the general criteria required for the diagnosis of any allergic syndrome.

EDITOR'S ABSTRACT.

NONSUPPURATIVE INTRACRANIAL COMPLICATIONS OF OTITIS MEDIA. ADAMS A. MCCONNELL, Brit. M. J. **2**:659 (Oct. 2) 1937.

Nonsuppurative intracranial complications of otitis media are of two kinds: (1) an encephalitic lesion, which gives rise to both focal and general symptoms, and (2) derangement in the amount or circulation of cerebrospinal fluid, which results in an increase in intracranial pressure without focal symptoms. Nonsuppurative encephalitis is rare as compared with abscess of the brain. The diagnosis cannot be made except after exploration for abscess of the brain has given negative results. Recovery is the rule.

Derangements of the cerebrospinal system complicating otitis media are of two types. One is the "otitic hydrocephalus" described by Symonds in 1931. The symptoms are intermittent headache and papilledema. The cerebrospinal fluid is increased in amount but is normal in other respects. One or more drainages by lumbar puncture are curative. The second type is obstruction of the circulation of the cerebrospinal fluid. If the obstruction is at the outlet of the ventricles an internal hydrocephalus results. If one of the cisterns of the posterior fossa becomes obstructed there is a local collection of fluid under pressure. In either case the symptoms are the same. Lumbar puncture is neither curative nor safe in the presence of obstructive hydrocephalus. Since it is difficult or impossible to distinguish between an increase in the amount of fluid and an obstruction to the circulation, the proper treatment is drainage by ventricular puncture. If communicating hydrocephalus is found, lumbar puncture may be used in treatment. Surgical treatment is indicated in the obstructive type of hydrocephalus.

ECHOLS, New Orleans.

THE EARLY DIAGNOSIS OF INTRACRANIAL TUMOUR. F. M. R. WALSHE, Brit. M. J. **2**:889 (Nov. 6) 1937.

The clinical course of an intracranial tumor is likely to follow one of four main lines of development, the first of which is characterized by the recurrence of generalized epileptic fits. When such convulsions make their appearance in a

middle-aged person they should give rise to suspicion of tumor. Jacksonian fits may also occur as an early sign of tumor of the brain, but are less common. A more frequent mode of onset is that in which there develop signs and symptoms of increased intracranial pressure, namely, headache, vomiting and papilledema. The headache often awakens the patient in the early morning hours and is most severe at that time. Slowing of the pulse is not a frequent sign except in the case of a rapidly growing glioma. A high degree of papilledema may coexist with normal vision. Another mode of evolution is that in which there is evidence of a progressive local lesion. Slowly developing weakness of one side of the body is an example. However, paralysis agitans without tremor may give a similar picture. Walshe mentions 2 such cases in which the patient was subject to craniotomy. The fourth mode of onset described by Walshe is seen in cases of metastatic carcinoma of the brain. The multiple lesions may produce marked disturbance characterized by muttering, delirium, gross defect of memory and confusion. Meningeal involvement by metastases may produce signs which are suggestive of meningitis. Rarely, carcinoma cells have been seen in the spinal fluid.

ECHOLS, New Orleans.

THE EARLY DIAGNOSIS OF INTRACRANIAL TUMOR. NORMAN M. DOTT, Brit. M. J. **2**:891 (Nov. 6) 1937.

To be of clinical value a diagnosis must answer three questions: Is there a tumor? Where is it located? What is its probable nature? The histologic character of the tumor and its exact boundaries should be determined if possible. Roentgenography is one of the special means of examination that may give information of great importance. Localizing signs include calcification in the tumor, erosions or hyperostoses of the skull and erosions of the foramens of cranial nerves. Calcification in the falx and pineal gland permit recognition of a shift of the structures in the midline. Widening of suture lines, decalcification of the clinoid processes and accentuation of the digital markings are signs of increased intracranial pressure. The danger of lumbar puncture in cases of intracranial tumor has been overemphasized; if it is done by a neurologist valuable information may be obtained. Dott has employed ventriculography in about 40 per cent of cases. It should be followed immediately by craniotomy. Encephalography is usually employed only to supplement a ventricular injection of gas which has inadequately filled the ventricles. Cerebrovascular roentgenography is also advocated. Colloidal thorium dioxide is injected into the exposed internal carotid artery. The arterial displacements around a tumor may give exact information as to its extent. This method is of special value in cases in which aneurysm is suspected. As it is usually undesirable to operate on a patient with malignant glioblastoma, a specimen for biopsy may be obtained through a trephine opening with the exploring cannula to verify the diagnosis. If the clinical examination is supplemented by one or more of these special procedures, a correct diagnosis of the tumor and its location can be made in 99 per cent of cases. The histologic nature of the tumor can be forecast with reasonable certainty in 70 per cent of cases.

ECHOLS, New Orleans.

Peripheral and Cranial Nerves

SYMPATHETIC INNERVATION OF THE EXTERNAL SPHINCTER OF THE HUMAN BLADDER. PAUL C. BUCY, C. HUGGINS and DOUGLAS N. BUCHANAN, Am. J. Dis. Child. **54**:1012 (Nov.) 1937.

Bucy and his associates report the case of a boy aged 14 with marked retention of urine and overflow incontinence, associated with spina bifida occulta and myelodysplasia. An abdominal operation was performed, at which section of the presacral (pelvic sympathetic) nerve was carried out. During the operation the peripheral end of the cut nerve was stimulated by a faradic current, and the

cystoscopist reported the following observations: "(*a*) contraction of some 'sphincteric' structure, probably smooth muscle of the prostatic urethra and the prostate at the junction of the prostatic and membranous portions of the urethra, . . . termed the 'sympathetic external sphincter'; (*b*) diminution in the size of the verumontanum, possibly as a result of vasoconstriction, and (*c*) emission of prostatic and seminal fluid." The authors believe that the improvement in this case, sustained over a period of three years, is due to relaxation of the sympathetically innervated sphincter muscle rather than to release of the inhibitory effect of these nerves on the detrusor muscle.

WAGGONER, Ann Arbor, Mich.

RETROBULBAR NEURITIS IN PELLAGRA. M. FINE and G. S. LACHMAN, Am. J. Ophth. **20**:708 (July) 1937.

Fine and Lachman observed 3 patients suffering from pellagra who had impaired vision due to retrobulbar neuritis. In the first patient retrobulbar neuritis was diagnosed several weeks before signs of pellagra appeared. In each case the presence of lesions of the skin led to the correct diagnosis. With the present state of knowledge of pellagra, one can only speculate on the relationship of the pellagrous syndrome to the visual disturbances. The etiology of the disease is still unsettled. Since vitamin B_2, or G, was separated from the antineuritic factor B_1, it has become more and more apparent that even vitamin G is a complex of various factors, the number and nature of which are not understood. The history of patients with "alcohol pellagra" is usually that of chronic alcoholism over many years with the appearance of pellagra-like symptoms after a spree lasting several weeks. It has been suggested that the important factor is undernutrition and damage to the alimentary tract from the alcohol, interfering with absorption. When the ocular disturbance associated with pellagra is considered, the problem of the role of alcohol becomes more significant, in view of the relative frequency of so-called tobacco-alcohol amblyopia. The association of tobacco with ethyl alcohol in producing injury to the visual fibers is constant. There has been an increasing tendency to regard alcohol as an exciting factor in tobacco amblyopia. Recently, the role of chronic alcoholism in peripheral neuritis has been questioned. It is not improbable that a relationship such as exists between vitamin B_1 deficiency and the peripheral nervous system may also exist between vitamin B_2 (G) deficiency and the central nervous system, of which the optic nerve is a part, and that in each case the alcoholism plays only an indirect part. Such a quantitative relationship offers an explanation of the fact that some alcoholic addicts never suffer from amblyopia, while other relatively moderate drinkers suffer serious insult to the visual fibers. The question arises whether in many cases "alcohol and tobacco" amblyopia is not complicated by a deficiency of vitamin G.

EDITOR'S ABSTRACT.

ACUTE LABYRINTHITIS WITH COMPLICATING LATE FACIAL PARALYSIS. ANDERSON HILDING, Arch. Otolaryng. **26**:93 (July) 1937.

Hilding reports the case of a child aged 6, subject to repeated attacks of otitis, who was suddenly stricken with vertigo and earache on the right side. The next day, vomiting, tenderness over the mastoid, marked rotatory nystagmus to the left, impairment of hearing and pus in the auditory canal were noted. Within forty-eight hours after the first symptoms, a dead labyrinth was found. The temperature was 102 F., with definite stiffness and rigidity of the neck. The spinal fluid pressure was 6 mm., and the cell count, 800. A Neumann operation on the labyrinth was performed. After operation there was a free discharge of spinal fluid. The cell count of the spinal fluid decreased from 1,890 to 19, and the patient progressed well until the twenty-seventh day, when right facial palsy developed. On exploration a sequestrum of the labyrinth, involving the fallopian tube, was noted. It was removed, leaving the facial nerve exposed. Convalescence was rapid and uneventful; facial movements began on the fourth day after operation and by the ninth were entirely normal.

HUNTER, Philadelphia.

TOXIC OPTIC NEURITIS RESULTING FROM SULFANILAMIDE. P. C. BUCY, J. A. M. A. **109**:1007 (Sept. 25) 1937.

Bucy believes that a case of toxic neuritis resulting from the administration of sulfanilamide or any of the related drugs has not previously been reported in man. Likewise, manifestations of involvement of the central nervous system other than mental confusion have not been observed. The majority of toxic manifestations that have resulted from the use of these drugs in man are concerned with the blood. Fever resulting from the administration of these drugs has also been recorded. Various symptoms, such as urinary irritation, lassitude and dizziness, nausea, headache and abdominal discomfort, have also been noted. Except in Borst's case, the toxic manifestations have been mild and have subsided when administration of the drug was discontinued. However, in a few instances the developments have been serious and severe, if not fatal. It is obvious that sulfanilamide, though apparently a therapeutic agent of great value, has toxic qualities of no little import which must be reckoned with. A case is cited in which toxic optic neuritis apparently developed as a result of the administration of sulfanilamide. The fact is pointed out that some persons seem to tolerate the drug poorly and that with the development of any of the more severe toxic manifestations the drug should be withdrawn at once. In view of the frequency with which the hematopoietic system is involved, it appears advisable to make blood counts frequently, if not daily, on all patients receiving this drug. The case presented is that of a girl with osteomyelitis of the ilium who was given sulfanilamide on three occasions. After the first two administrations there appeared headache, cyanosis, diarrhea and a choking sensation. After administration of a single tablet (0.3 Gm.) on the last occasion, there was severe loss of vision due to toxic optic neuritis. In each instance the symptoms subsided rapidly after withdrawal of the drug. The case emphasizes the importance of not administering sulfanilamide and any sulfate simultaneously.

EDITOR'S ABSTRACT.

PARALYSIS OF DENTAL ORIGIN: ATTEMPT AT EXPLANATION OF PERIPHERAL FACIAL PARALYSIS. P. PANNETON, Presse méd. **45**:1356 (Sept. 25) 1937.

Panneton observed 2 patients with facial paralysis of the peripheral type which developed after dental extractions. In 1 case the tooth extracted was an upper premolar, and in the other, a lower. The author investigated how the extraction of a tooth may lead to facial paralysis; that is, what relation exists between the facial nerve in its passage through the fallopian aqueduct and the upper and lower premolar regions of the same side. He investigated four possible connections: By contact and by vascular, lymphatic and nerve channels. After ruling out the connections by direct contact and by the vascular and lymphatic passages, he studied the nerve connections. He reaches the following conclusions: 1. In cases of facial paralysis of dental origin, the point of transmission is observed at the level of the two superficial petrosal nerves, the large and the small, both of which enter the geniculate ganglion in contact with the facial nerve. 2. In a large number, and perhaps the majority, of cases, facial paralyses of the peripheral type, which are generally referred to as *a frigore* in origin, are of sympathetic origin. 3. These forms of paralysis are dependent on deep lesions of the facial nerve. 4. The peripheral facial paralyses are in most cases, if not always, the result of circulatory disturbances in the vasa nervorum of the seventh cranial nerve, particularly in the region of the geniculate ganglion, which are produced by a physiologic lesion of the cephalic portion of the sympathetic chain.

EDITOR'S ABSTRACT.

CIRCUMSCRIBED LESION OF THE FACIAL NERVE IN THE AQUEDUCT OF FALLOPIUS. E. FALCAO, Rev. de neurol. e psychiat. de São Paulo **3**:27, 1937.

In Falcoa's case an umbrella rib was trust through the external auditory meatus, wounding the facial nerve in the wall of the middle ear. Suppuration

occurred, and facial palsy developed, beginning with the lips and spreading to the forehead. Eighteen days after the accident, improvement began in the forehead and spread to the chin. The author points out that this fact supports the contention of Moure that the fibers for the lower part of the face surround those for the forehead like a sleeve.

PUTNAM, Boston.

Cerebrospinal Fluid

THE EFFECT OF THE INTRAVENOUS INJECTION OF HYPERTONIC DEXTROSE SOLUTION UPON THE CEREBROSPINAL FLUID PRESSURE IN CASES OF BRAIN TUMOR. F. G. LINDEMULDER, Am. J. M. Sc. **194**:554 (Oct.) 1937.

Lindemulder studied the effect of intravenous injection of hypertonic solution of dextrose in 6 cases of tumor of the brain, 2 cases of gumma of the brain and 1 case of an old fracture of the skull. From 50 to 100 cc. of a 50 per cent solution of dextrose was injected slowly. In only 1 case was the cerebrospinal fluid pressure reduced without reaching at some time during the experiment a higher level than the original pressure. In only 1 case was the pressure lower at the end than at the beginning of the examination. The explanation offered is that the pressure is elevated by oxidation of the solution of dextrose injected, which drains the fluid from the body tissues and releases it by osmosis to the circulation.

MICHAELS, Boston.

REDUCTION OF INTRACRANIAL PRESSURE IN CEREBRAL INJURY BY INTRAVENOUS USE OF HYPERTONIC SUCROSE SOLUTION. H. JACKSON, D. DICKERSON and A. GUNTHER, Ann. Surg. **106**:161 (Aug.) 1937.

Jackson and his associates selected stuporous or comatose patients who showed signs of contusion of the brain (increased intracranial pressure and bloody fluid), usually with fissured fracture of the skull, as subjects for reduction of intracranial pressure by injection of a 50 per cent solution of sucrose. The patients were placed in the lateral position with the head on a level with the spine. In restless patients, local procaine anesthesia was used for the introduction of the spinal needle. The Queckenstedt test was applied to determine the patency of the cerebrospinal system. The solution was injected slowly into the median basilic vein of the forearm in amounts of 100, 200, 300 and 400 cc. Readings were then repeated, with the spinal needle attached to the mercury manometer, at varying intervals up to forty-eight hours. In 8 patients with cerebral injury accompanied by severe trauma the average reduction in pressure was 50 per cent; the least reduction was 16 per cent, and the greatest, 66 per cent. The reduction was maintained for six hours, and in some cases for as long as twenty-four hours. From 200 to 300 cc. of solution is necessary in most instances to produce such reductions because sucrose has only one-half the osmotic pressure of dextrose. In 3 patients with severe disturbance, 1 of whom was dying, there was no reduction. In 2 patients there was an increase in pressure. A slight increase in pressure, from 34 to 36 mm. of mercury was produced by 100 cc. of the solution after four hours. In the other subject, 400 cc. caused an increase of from 11 to 16 mm. of mercury after two hours. In both subjects, a reduction was afterward obtained by the withdrawal of cerebrospinal fluid. As compared with the action of dextrose, the reduction in spinal pressure with the sucrose solution was greater, in some cases up to three times that produced by dextrose. There was no secondary increase in cerebrospinal pressure, except in 2 instances, and no toxicity, and with a few exceptions, the patients were relieved from headache and restlessness. No increase in the sugar content of the cerebrospinal fluid was noted. Hypertonic solution of sucrose may be used as an adjunct in cases of severe edema of the brain in which spinal drainage is not successful and in cases of multiple fracture of the pelvis or extremities in which spinal drainage is difficult or impossible. In cases

in which spinal drainage is not productive of a marked fall in pressure, the edema of the brain may be pronounced, and the use of hypertonic solution of sucrose may be of greater benefit. Sucrose acts by withdrawing water from all the body tissues into the blood, which, in turn, throws off both fluid and sucrose through the kidneys by active diuresis. Similar withdrawal of fluid may be obtained with hydragog cathartics.

EDITOR'S ABSTRACT.

INTRACRANIAL PRESSURE WITHOUT BRAIN TUMOR. W. E. DANDY, Ann. Surg. **106**:492 (Oct.) 1937.

During the last seven years, Dandy encountered 22 cases in each of which the signs and symptoms of intracranial pressure were indubitable; yet in none was there an intracranial tumor or a space occupied by a lesion of any kind. Almost without exception, a clinical diagnosis of unlocalized cerebral tumor was excluded by ventriculography. All the patients complained of headache; most of them, of nausea, vomiting, diplopia and dizziness, and many, of loss of vision; objectively, there were in every instance bilateral papilledema and usually hemorrhages in one or both eyegrounds to indicate that intracranial pressure was present. In each case the intracranial pressure was demonstrated objectively, and was usually actually measured by ventricular or lumbar puncture. The subsequent demonstration of pressure over a period of months or years is merely a matter of inspecting the site of the subtemporal decompression to which most of the patients were subjected for treatment, with success. The increased intracranial pressure may last only a few months, but at times it may persist for years. Curiously, the decompression is almost never consistently at its maximal fulness but is intermittent, and the pressure may come and go with surprising rapidity—from one extreme to the other in a few minutes. The cause of the sudden changes—indeed, the cause of the increased pressure itself—is unknown. It can be reasoned with safety that the increased intracranial pressure is dependent on the content of the intracranial fluid. The only other possible explanation of the increased pressure is variation in the intracranial vascular bed, probably through vasomotor control. That the increased pressure usually sets its limit within the bounds of relief afforded by a subtemporal decompression is indeed surprising. The periodic nature of the attacks and the permanence of cure of 4 persons known to have received no treatment lead to the suspicion that this condition may be common, that only the most severe grades are encountered by the physician and that many transient, unexplainable headaches may really be instances of this condition, though in lesser degree.

EDITOR'S ABSTRACT.

PROTEIN IN CEREBROSPINAL FLUID. G. PHILLIPS, M. J. Australia **2**:179 (July 31) 1937.

In tabes and meningovascular syphilis the normal protein content of cerebrospinal fluid, from 20 to 40 mg. per hundred cubic centimeters, is increased to from 30 to 80 mg., and at the same time there is a disproportionate increase in the globulin fraction. Phillips states that the protein content is increased in all meningeal infections; in septic and tuberculous meningitis the protein may range from 50 to more then 150 mg. per hundred cubic centimeters. In disseminated sclerosis also, there is usually a slight increase in protein content. In practically every case of cerebral abscess an increase in protein will be found, even when the abscess is deeply situated. The explanation of this is probably the fact that a centrifugal circulation is provided by the Virchow-Robin spaces adequate to enable the discharge of protein from edematous areas of cerebral tissue surrounding the abscess. Even after apparently adequate surgical drainage of a cerebral abscess, a guarded prognosis should be given while the protein remains at a level above that of high normal. Most intracranial neoplasms, particularly if they arise from the arachnoid and, more particularly, if they are situated in the

posterior fossa, will cause an increase in protein in the cerebrospinal fluid. All neoplasms of the posterior fossa, except cholesteatoma, cause an increase in protein content, whether they are intracerebellar or extracerebellar in origin. This is due to the relatively smaller size of the cerebellum and its intimate contact with the fluid not only in the convexities but also in the fourth ventricle. Above the tentorium, increase in protein is most likely to be caused by a meningioma or by any other cerebral growth which has arisen at or grown into contact with the surface of the hemisphere or the ventricular ependyma. In the case of growths in contact with the ventricles, the great bulk of protein is added to the cerebrospinal fluid after it passes out of the ventricular system into the subarachnoid spaces. Estimation of the protein in specimens of fluid taken from both lateral ventricles may be of localizing significance, since a tumor in contact with one ventricle may produce an increase of protein in the fluid in that ventricle with little or no increase in the fluid from the contralateral ventricle. In the third ventricle the well known colloid cyst does not cause any increase in protein; this knowledge may be of value in differentiation of this condition from tumors in the same ventricle, particularly spongioblastoma. EDITOR'S ABSTRACT.

VIRULENCE OF CEREBROSPINAL FLUID IN COURSE OF SIMPLE MUMPS. V. DE LAVERGNE, P. KISSEL and H. ACCOYER, Bull. et mém. Soc. méd. d. hôp. de Paris **53**:1276 (Nov. 15) 1937.

Lavergne and his collaborators inoculated 8 rabbits suboccipitally with 1 cc. of cerebrospinal fluid from 8 patients suffering from simple parotitis. The changes in the cerebrospinal fluid were observed by punctures at intervals of four days for three or five weeks. At the end of the experiment, microscopic studies of the brains were made. Seven rabbits reacted with persistent hypercytosis (hyperlymphocytosis) during the first ten days. The reaction diminished in the course of the experiment and showed a late recrudescence in 5 animals. The brains of the 5 rabbits that had early and late hypercytotic reactions showed microscopic changes characteristic of neuraxitis and, in 2 cases, also of parotitic radiculitis. The brains of the 2 rabbits that had early, but not late, hypercytotic reaction showed inflammation, but no anatomic changes. In the rabbit in which the cytologic reaction of the cerebrospinal fluid was normal meningitis did not develop. The authors conclude that the cerebrospinal fluid of patients who are suffering from simple parotitis is virulent for rabbits in almost all cases. The cerebrospinal fluid is virulent, although the patients do not show clinical symptoms of meningitis and the fluid does not show important cytochemical alterations. Absence of meningitis complicating parotitis in man does not indicate absence of the virus of parotitis in the brain. Development of meningitis in association with mumps does not show an abnormal location of the virus of parotitis, which is present in the cerebrospinal fluid in the course of simple parotitis in all cases. The development of clinical meningitis is probably due to an unknown cause which is independent of the presence or absence in the cerebrospinal fluid of the virus of parotitis. EDITOR'S ABSTRACT.

Treatment, Neurosurgery

SUBARACHNOID INJECTION OF ALCOHOL FOR RELIEF OF INTRACTABLE PAIN, WITH DISCUSSION OF CORD CHANGES FOUND AT AUTOPSY. W. P. PEYTON, E. J. SEMANSKY and A. B. BAKER, Am. J. Cancer **30**:709 (Aug.) 1937.

Peyton and his co-workers studied at necropsy the spinal cords of 4 patients with incurable malignant tumor who lived from three to six months after subarachnoid injection of alcohol for relief from pain. A series of experimental injections in 5 dogs were also made, but the results were not satisfactory. It was difficult, or impossible, to obtain even approximately the same conditions as

obtain in man and impossible to determine whether a satisfactory injection was accomplished, that is, one which would relieve pain if it were present. Microscopic study of the spinal cords indicated that relief from pain, when it occurs, is due to destruction of the posterior rootlets, but that there is also extensive degeneration of the posterior columns of the cord. A satisfactory result was obtained in at least 33, and in not more than 51, per cent of 33 patients. Serious complications occurred in 2 patients, 1 of whom, however, had preexisting paralysis due to a progressive lesion of the cord. The partial paralysis was precipitated into complete paralysis by the injection. A sufficient proportion of patients are benefited to justify the slight risk of serious injury to the spinal cord, provided the procedure is limited to the treatment of intractable pain associated with malignant disease of hopeless prognosis.

EDITOR'S ABSTRACT.

A METHOD OF DRAINING CEREBRAL ABSCESSES. J. M. ROBISON, Arch. Otolaryng. **26**:49 (July) 1937.

Robison reports a new method of treating cerebral abscess. In the usual operation, particularly for abscess in the acute stage, a large incision is made in the dura and the abscess is freely evacuated, the edematous brain tissue immediately filling the abscess cavity. This leaves no cavity or area in which to place a drain. The closing in of the walls of the abscess leads to pocketing of the infection. Since also in the area of cerebritis surrounding the abscess the perivascular spaces are filled with lymphocytes and the excess fluid cannot be carried away, the nutrition of the brain substance is impaired, and necrosis ensues. This change in the area surrounding the abscess probably accounts for the symptoms, often fatal, which occur several days after the operation.

Robison advocates the following procedure: The skull is removed from the dura over the area of the abscess, enough being taken away to allow the dura to bulge into the opening. The pressure of the brain against the dura around the margins of the bone defect precludes the possibility of pus entering the subdural space as it is drained from the abscess. In the center of the decompressed area a small incision is made through the dura parallel to any vessels present. A bayonet forceps is then passed into the abscess cavity. As soon as a little pus has escaped, a long strip of rubber tissue, about ¼ inch (0.6 cm.) wide, is packed along the bayonet forceps into the abscess cavity. As more pus escapes more tissue is introduced, the amount used being determined by the amount of pus evacuated. The object is to fill the abscess cavity as nearly as possible with rubber tissue before the walls of the cavity collapse. The terminal end of the rubber tissue is then made secure. The advantages of this procedure are avoidance of sudden release of pressure and prevention of pocketing and of sudden changes in intracerebral pressure. When broken-down clots or necrotic parts of the wall are present, it may be necessary to insert rubber tubing several days after the abscess is opened. The rubber tissue is nonirritating. It may be extruded. It should be removed gradually in from four to six months.

HUNTER, Philadelphia.

SULFANILAMIDE THERAPY IN MENINGOCOCCIC MENINGITIS. L. J. WILLIEN, J. A. M. A. **110**:630 (Feb. 26) 1938.

After the favorable report by Schwentker, Gelman and Long, Willien began the use of sulfanilamide for meningococcic meningitis. Treatment of 5 patients, 1 of whom had had a recurrence of the disease, is reported. There was no selection of patients; the intensity of the infection varied from moderate to severe; the ages of the patients were from 1½ to 26 years. The technic of Schwentker, Gelman and Long was used at first; after confirming their results, Willien began the use of sulfanilamide by oral administration alone following an initial sub-

cutaneous injection that was given to saturate the body tissues and build up a high concentration in the blood. The clinical response of the patients to treatment with sulfanilamide was satisfactory in every case. The possibility of being able to cure meningococcic meningitis by the administration of sulfanilamide by mouth only will be of untold benefit, through elimination of the time, trouble and expense of intraspinal and intravenous therapy, together with the danger of protein shock and the discomfort of serum sickness. The economic saving is of great importance. An example of this is shown in case 2. A total of 610,000 units of antitoxin was administered, 82.5 cc. of one brand of serum and 30 cc. of another, over a period of forty-one days and at a cost of more than $500 for the serum and antitoxin alone, which failed to effect a cure. Two dollars worth of sulfanilamide effected a cure in fourteen days. A reaction characterized by acidosis, cyanosis and a morbilliform rash over the extremities was observed in case 3. This subsided promptly in less than twenty-four hours after the drug was discontinued. No other reactions were observed in any of the cases. Continuation of the drug in reduced doses for from ten days to two weeks after symptoms of the disease subside is important, as the drug is bacteriostatic rather than bactericidal and recurrences such as occurred in case 3 are likely. The author's technic of administration of sulfanilamide is based on consideration of the absorption and excretion of the drug and is as follows: 1. An initial subcutaneous injection of a large dose of the saturated (0.8 per cent) solution is given in amounts of approximately 0.05 Gm. per kilogram of body weight. 2. The drug is administered by mouth every four hours day and night. 3. The dose is graduated from an upper limit of 15 grains (1 Gm.) every four hours, depending on the size and age of the patient and the severity of the infection. 4. The drug is continued, in reduced dose, for about ten days after the symptoms and laboratory readings have returned to normal. 5. Sodium bicarbonate is given grain for grain with sulfanilamide in order to combat acidosis. 6. Magnesium or sodium sulfate is not given in order to avoid sulfhemoglobinemia.

TREATMENT OF ACUTE POLIOMYELITIS BY INTRAVENOUS INJECTION OF HYPOTONIC SALT SOLUTION. G. M. RETAN, J. Pediat. **11**:647 (Nov.) 1937.

Retan maintains that acute poliomyelitis can be influenced favorably by the intravenous injection of hypotonic solution of sodium chloride. The statement is based on the following experience: Ten patients with paralysis of the respiratory muscles were treated, and all recovered. Improvement in respiratory function is both objective and subjective and occurs during the actual period of treatment. One of the patients showed complete paralysis of both the diaphragm and the intercostal muscles before treatment. Six patients with paralysis of deglutition recovered promptly. All patients so treated were able to drink fluids after the first treatment, an event which cannot be explained on the basis of coincidence, as paralysis of the throat does not thus improve in untreated patients. This treatment will not prevent the development of paralysis in every instance. This is particularly true of the ascending (Landry) type. However, the Landry type of respiratory paralysis, of which the patient dies, does yield to the treatment in some instances, and it is therefore possible to save the lives of these patients. More vigorous treatment is indicated in this group. Weakness of the muscles of the extremities, without actual paralysis, has improved promptly, and the author has often seen reflexes return after treatment which before had not responded to stimuli. Actual paralysis of the muscles of the extremities does not improve. However, treatment of this group is advised if the disease is "active," with the hope of preventing further loss of function. Paralysis and death have been prevented in rhesus monkeys which have been infected with many times the lethal dose of virus, all the animals which served as controls having died after complete skeletal paralysis.

EDITOR'S ABSTRACT.

STUDY OF TEMPORARY USE OF THERAPEUTIC DOSES OF BENZEDRINE SULFATE IN ONE HUNDRED AND FORTY-SEVEN SUPPOSEDLY NORMAL YOUNG MEN (MEDICAL STUDENTS). H. B. GWYNN and W. M. YATER, M. Ann. District of Columbia **6**:356 (Dec.) 1937.

To study the immediate effects of benzedrine sulfate in therapeutic doses, Gwynn and Yater gave half of 151 students 10 mg. tablets of benzedrine sulfate after breakfast and after lunch for three days; the other half were given tablets of lactose. After a period of five days the preparations were reversed, but the students were not informed that they were receiving another kind of tablets. Altogether, 147 students took the benzedrine tablets, and all 151 students took the lactose tablets. All 147 students who took the benzedrine reported reactions of some kind from the use of the drug. Only 16 of the 151 students who took the lactose reported reactions which they thought were due to it. In answer to the specific question: "Did you feel fatigued, peppy or as usual?" 113 stated that they felt "peppy." In answer to questions as to any change in mood, 72 students reported that they became exhilarated. Forty-two students answered that they became more talkative. Sixty-one reported that they had an increase in power of concentration while taking the drug, and 8 reported decrease. Eighty-one stated that they were more nervous. Seventy-six students reported dryness of the throat. One hundred and twenty-six students suffered from insomnia, and 57 students reported decrease in appetite. Only 38 students expressed a desire to continue use of the drug, and 80 per cent of these qualified the answer by stating that they would like to use it at time of examinations and when it was necessary to stay awake. Hypertension, coronary arteriosclerosis and a state of manic excitement are definite contraindications to use of the drug. Benzedrine has been advocated for use as a local astringent; in treatment of narcolepsy, persistent states of fatigue (nervous exhaustion), postencephalitic parkinsonism, arterial hypotension, gastrointestinal spasm and overdoses of barbiturates; in preparation of persons for periods of unusual mental or physical exertion; as an adjunct to the action of atropine, stramonium and scopolamine, and in attacks of migraine. It appears that the use of the drug may be permitted, or even prescribed, for normal persons who suffer from lack of self confidence or mild depression and who deem it advisable to overcome these drawbacks temporarily. Similarly, the drug might be permitted to persons who are required to engage in tests requiring mental alertness, or perhaps in competitive physical activities. The drug is only an emergency measure; after the emergency has passed an adequate period of rest must be available. Benzedrine is apparently not conducive to habit formation. Although it is apparently not dangerous, it appears that the dose of 20 mg. a day is too much for the average normal person because of the insomnia and other unpleasant side effects.

EDITOR'S ABSTRACT.

TREATMENT OF ACQUIRED DEFECTS OF THE SKULL. J. HOGARTH PRINGLE, Brit. M. J. **2**:1105 (Dec. 4) 1937.

During the World War Pringle placed celluloid plates in the skulls of 18 soldiers who had acquired defects of the skull. Ten of these men were examined during 1937 (twenty or twenty-one years later). All celluloid plates were still in place but 1. This plate had been removed after seven years because of infection. The celluloid employed was 1/16 inch (1.5 mm.) thick. Pringle reports an additional case in which a celluloid plate had been present for forty years.

ECHOLS, New Orleans.

TREATMENT OF CUSHING'S SYNDROME WITH LARGE DOSES OF OESTRIN. A. MORTON GILL, Lancet **2**:71 (July 10) 1937.

Three patients with Cushing's syndrome were treated with the daily administration of from 100,000 to 200,000 international benzoate units of estrogen for from one and one-half to two months, on the principle that if the basophilic cells

of the pituitary can be inhibited some patients may secure relief from their symptoms. No effect was observed objectively, but the severe headaches were "either abolished or greatly improved."

KRINSKY, Boston.

BULGARIAN TREATMENT OF POST-ENCEPHALIC PARKINSONISM. F. J. NEUWAHL and C. C. FENWICK, Lancet **2**:619 (Sept. 11) 1937.

The basis of the Bulgarian treatment lies in the difference in the root of belladonna used. It is described as "the root of the Solanaceae from Bulgaria." The advantages of its use are the greater tolerance for the drug, the slower absorption and, as a result, the more prolonged action, with lower toxicity. The toxic manifestations of the Bulgarian treatment are vertigo, dryness of the mouth and mydriasis.

The preparation is a decoction of 30 Gm. of the root and rhizome of belladonna in 600 cc. of dry white wine, which contains from 10 to 12 per cent of alcohol. The maceration lasts five or six hours; the mixture is then boiled for fourteen minutes and filtered through absorbent cotton. The dose is controlled by the physician and is not standardized. Panegrossi starts with from 2 to 3 cc. at 11 p. m. and increases the dose daily from 1 to 3 cc. until 20 cc. is reached. The dose is then divided, one-half being given at 11 a. m. and the other at 11 p. m. It is safe to give as much as 60 cc. of the decoction daily to patients without gross organic disease. The diet is chiefly lactovegetarian. Alcohol, coffee, spices and tobacco are forbidden.

Neuwahl and Fenwick treated two men, one aged 54, and the other 65. The first patient had had encephalitis lethargica in 1922, with parkinsonian symptoms shortly thereafter. Atropine and scopolamine were equally ineffective. The patient was given daily 5 cc. of the decoction of Bulgarian belladonna root; a daily maximum of 90 cc. was reached, when vertigo developed. The optimum dose in this case was 60 cc.; the general condition improved within eight days. The patient was able to dress and feed himself, as well as to walk a half mile, after five weeks. The tremor decreased in severity, and the palpebral spasm disappeared after two weeks.

The second patient had had parkinsonism for twenty years. He improved after taking 15 cc. a day. Although the postencephalitic symptoms improved, treatment had to be discontinued, since the patient presented a mental problem as well.

The authors recommend the Bulgarian treatment because of the more beneficial results, the less frequent danger of complications and the low cost.

KRINSKY, Boston.

SCHIZOPHRENIA AND ITS TREATMENT BY INSULIN AND "CARDIAZOL." R. S. ELLERY, M. J. Australia **2**:552 (Oct. 2) 1937.

Ellery discusses the many methods of previous empiric treatment of schizophrenia and concludes that the whole point in the empiric organic procedures of the past is that, while it is better to apply treatment that will achieve sporadic success and a certain amelioration of symptoms than to stand by resignedly, not one of the methods is capable of giving results consistently better than those which are liable to occur spontaneously, if one accepts the dictum that such remissions occur in approximately 20 per cent of unselected schizophrenic patients. Complete details are given of insulin shock (Sakel) and metrazol convulsions (Meduna) therapy. To the unfamiliar observer, hypoglycemic shock therapy may look particularly dangerous and somewhat cruel. However, in the hands of a competent physician who has familiarized himself with all aspects of the treatment, the dangers are often more apparent than real. From the patients' point of view the treatment is neither perilous nor painful. Amnesia prevents them from remembering any of the more distressing symptoms. Almost invariably, patients gain weight and begin to feel more physically fit. This, together with the return of lucidity, more than

compensates for any initial discomfort they may have experienced. With proper use of the insulin shock treatment one is now able to anticipate full remissions in from 70 to 80 per cent of schizophrenic patients whose illness is of less than six months' duration and in approximately 60 per cent of those whose mental disorder has persisted for not more than eighteen months at the time of treatment. For patients who have been ill for longer than eighteen months the chance of achieving a remission diminishes rapidly as the length of the illness increases and as defect symptoms are manifest; but, in addition to the not altogether negligible number who seem to recover, nearly 50 per cent show varying signs of improvement. With metrazol therapy a good remission has been obtained in 50 per cent of unselected patients, the length of whose illness varied from one week to ten years. In patients with especially early stages, before the onset of permanent symptoms of mental deterioration, the reaction to this form of treatment has been favorable, and Meduna states that he has brought about a remission in 80 per cent of such patients. In a review of his results in individual cases, he finds that a good response may be anticipated in schizophrenic patients whose symptoms have not persisted for more than four years. He has failed to produce any good results in patients whose symptoms have persisted for a longer time. The best responses to metrazol have been achieved with the catatonic and hebephrenic types of schizophrenia. Until results are published, Meduna's figures must stand, a challenge to the modern psychiatrist confronted with the schizophrenic problem. Conclusions are drawn from both methods of treatment. The epileptic state is common to the two procedures, and a tentative suggestion is made that this may act by changing the biochemical milieu of the human organism in a beneficial way not yet understood, or that it may act merely as a shock, serving by its very intensity to bring the patient into a state of dependence, so that he can obtain benefit from the individual attention of those around him, as well as from the common sense psychotherapy consciously or unconsciously applied by the physician.

EDITOR'S ABSTRACT

ACTION OF SULFANILAMIDE IN PURULENT MENINGITIS OF STREPTOCOCCIC AND SECONDARY MENINGOCOCCIC ORIGIN. R. MARTIN and A. DELAUNAY, Presse méd. **45**:1406 (Oct. 6) 1937.

Martin and Delaunay, after a review of the literature, stress the slight toxicity of sulfanilamide, pointing out that the toxic dose is from twenty to fifty times greater than the curative dose. The therapeutic efficacy of sulfanilamide impressed the authors, especially in a case of purulent streptococcic meningitis. A boy aged 8 had an extremely severe meningitic reaction. Treatment with antimeningococcus serum proved ineffective. After bacterologic examination established the etiologic role of a hemolytic streptococcus, treatment with sulfanilamide was begun. Morning, noon and night, the boy was given tablets of 0.5 Gm. by mouth. At first the daily dose of sulfanilamide was 1.5 Gm., but it was increased to 2 Gm. and then to 3 Gm. Under the influence of this treatment, the extremely desperate illness had a favorable outcome. The authors cite others who obtained favorable results with sulfanilamide in the treatment of streptococcic meningitis.

EDITOR'S ABSTRACT.

RESULTS OF FEVER THERAPY IN CASES OF DEMENTIA PARALYTICA. H. REKER, Arch. f. Psychiat. **106**:617 (July) 1937.

This report deals with 703 patients with dementia paralytica studied during a period of nine years. Most of the patients were treated by various fever-producing agents, particularly malaria, recurrent fever and pyrifer (a nonspecific bacterial preparation). In terms of the results, the malarial treatment appeared to be the most successful, with 23.48 per cent of the patients showing good and 22.26 per cent incomplete, recovery, 27.13 per cent remaining in the hospital and 27.13 per cent dying either during the treatment or within the next two months.

In order to gain insight into the factors influencing the outcome of this treatment, a study was undertaken of the correlations between the clinical outcome and the following features. 1. Age. This seemed to have a definite effect on the results. The younger the patient the larger the number of good remissions. The older the patient the greater the probability of poor remissions, further progress of the disease or death. 2. Constitutional types. There appeared to be no significant relation between the physical type (Kretschmer) and the results of treatment. 3. Incubation period. The period elapsing between the original infection and the appearance of the first symptoms of dementia paralytica was of no significance, since there was a high percentage of both good remissons and deaths in cases in which this period was over twenty-five years. 4. Treatment for syphilis before fever therapy. When such treatment was given, the percentage of good remissions was defintely higher and the percentage of failures just as clearly lower than when no treatment was given. 5. Duration of the disease before fever therapy. This, too, was of great significance. The highest percentage of good recoveries and the lowest percentage of deaths occurred in patients who had had the disease less than six months. The reverse was true of patients who had had the disease more than eighteen months. 6. Clinical form of the disease. The best results were obtained in the depressive, the euphoric, the slightly demented and the expansive form of the disease. 7. Number of chills during the treatment. Patients with less than six chills showed poor results; the differences in the results for those who had more than six chills were not significant. 8. Average height of the fever. The best results were obtained in cases in which the fever ranged from 103.6 to 103.8 F. 9. Treatment for syphilis after fever therapy. The results were definitely better when chemotherapy for syphilis followed cessation of the fever.

MALAMUD, Iowa City.

USE OF NORMAL HUMAN SERUM IN MULTIPLE SCLEROSIS. E. STRANSKY, Wien. klin. Wchnschr. **50**:1093 (July 23) 1937.

Stransky based his therapeutic experiments with normal human serum on the hypothesis that multiple sclerosis is an infectious process. He admits that the infectious nature has not been proved as yet, but thinks that it is nevertheless possible. On the assumption that the blood of persons who remain free from the disease may contain humoral protective substances against the virus of multiple sclerosis, he decided to try the serum of such persons in the treatment of patients with multiple sclerosis. In view of the fact that multiple sclerosis develops usually in the period between puberty and the middle years of life and only rarely in persons over 50 years of age, he tried serum of persons over 50 years of age who had never shown signs of multiple sclerosis. The serum of such persons was subjected to the process necessary to insure its sterility and was placed in ampules of 10 cc. each. It was injected into the gluteal muscle of patients with multiple sclerosis. The dose never exceeded 20 cc. in one day. The interval between the injections was usually two days, rarely one day. In a few cases more than two days elapsed between the injections. The author cites several cases of multiple sclerosis in which this treatment produced favorable results. The quantity of serum that is required for an effect and the duration of the effect vary in different cases. The author shows that this treatment will require further investigation. He suggests that larger quantities of serum, or even direct blood transfusion, might be tried.

EDITOR'S ABSTRACT.

INSULIN SHOCK TREATMENT OF SCHIZOPHRENIA. P. PLATTNER and E. FRÖLICHER, Ztschr. f. d. ges. Neurol. u. Psychiat. **160**:735 (Jan.) 1938.

Plattner and Frölicher report on 67 patients treated with insulin shock at Basel, Switzerland. The series included 30 men and 37 women. The results were better for the women. The injections were always given intramuscularly. The daily dose was increased by from 10 to 15 units up to the onset of hypo-

glycemic shock. The patients were usually left in coma for an hour. Complete remissions were most often seen when the duration of treatment was two months, the number of injections of insulin less than forty and the number of hours of coma less than twenty-five. In most of the cases of failure the patients had been treated longer than those who recovered. Thirty patients had epileptic attacks during the treatment. There is no demonstrable relation between the number of hours of coma and the frequency of attacks. Fewer convulsive seizures were noted in patients who showed remissions (16 with 4 convulsions) than in those for whom treatment had failed (51 with 26 convulsions). Analysis of 131 attacks in 31 patients, including 1 nonschizophrenic patient with diabetes, showed that most attacks occurred one hundred and sixty minutes after an injection. Usually, subsequent attacks occurred later after injection. In 1 case, during the second course of treatment the subsequent attacks came on sooner after injection.

There were 16 patients in an early stage of the disease (duration up to one-half year). Four of these showed complete, and 6 good, remissions (improvement in 62 per cent). Three showed no response, and 3 improvement with persistent defects. The percentage of failures among the patients with an early stage of the disease in this series was greater than that in series reported by other investigators. Nine patients with a duration of illness up to one and one-half years were treated. Only 1 showed a remission. This patient had a favorable prognosis even without treatment, for the disease came on after severe pleuritis and there was some clouding of the sensorium, suggesting the probability of the existence of symptomatic schizophrenia. Of 15 patients with a chronic form of the disease with remissions, 5 improved. The attacks during treatment lasted about as long as previous ones from which there was spontaneous recovery. There was no improvement in any of the 7 patients with a chronic form of the disease without spontaneous remissions. This large percentage of failures does not agree with the figures in studies previously reported from Vienna and other places. The type of schizophrenia is important as regards the response to treatment. Good results were obtained in one-half the catatonic patients. In all cases motor excitement became less with the use of insulin. Of 7 patients with a paranoid form, 3 with a remittent course showed improvement. In 8 patients with features suggesting cyclothymia the results were poor. There was no complete remission. Two of the 4 patients with the acute form showed improvement with persistent defects. The best results were obtained in the patients with the so-called psychogenic type, in which marked psychogenic factors were present with the schizophrenic symptoms.

SAVITSKY, New York.

TREATMENT OF DYSTROPHIA ADIPOSOGENITALIS WITH GONADOTROPIC HORMONE FROM THE URINE OF PREGNANT WOMEN. P. PLUM, Acta med. Scandinav. **93**:65 (Sept. 7) 1937.

Plum reports his experiences with the intramuscular injection of a gonadotropic preparation in 5 cases of adiposogenital dystrophy, 2 cases of cryptorchidism and 1 case of adiposity. The preparation that he employed is extracted from the urine of pregnant women; it is said to be free from the estrogenic principle and is standardized on the basis of its luteinizing effect on mice. In the cases of adiposogenital dystrophy treatment with gonadotropic substance alone produced in from six to eight weeks marked growth of the genitalia, but no change in the metabolism or the distribution of fat. When this treatment was combined with thyroid therapy, marked loss in weight was obtained. In 1 case of cryptorchidism, without associated signs of endocrine disturbance, the treatment was followed by marked growth of the genitalia, but the testes did not descend in the course of treatment for two months. In another case of cryptorchidism, associated with adiposity and decreased metabolism, descent of the testes was obtained in two weeks. In a few instances the treatment caused slight tenderness at the site of injection; otherwise there were no untoward effects.

EDITOR'S ABSTRACT.

Cerebellum and Brain Stem

A Study of the Anatomy of Vertebral Thrombosis. Donald Sheehan and G. E. Smyth, Lancet **2**:614 (Sept. 11) 1937.

Sheehan and Smyth report the cases of two patients with a retro-olivary syndrome in which the symptomatology indicated occlusion of the posterior inferior cerebellar artery, although postmortem examination revealed thrombosis of the entire vertebral artery.

The earliest description of the retro-olivary syndrome was given by Taylor in 1871. The condition is characterized by dissociated sensory disturbance on the contralateral side of the body due to involvement of the spinothalamic tract, although the cervical region is spared in some patients. Occasionally there is an ipsilateral Horner syndrome in these cases.

The first case was that of a man aged 55 who complained of weakness of the left arm and a sensation of pins and needles on the right side of the body, followed by inability to swallow the saliva. There was no loss of consciousness at any time. Examination of the patient revealed that the left pupil was smaller than the right, with narrowing of the palpebral fissure on the same side. There were coarse nystagmus when the patient looked toward the right and slight nystagmus when he looked toward the left. No sensory impairment was noted over the face, but there was loss of "common sensation" on the left side of the tongue. Taste was intact on both sides of the tongue. The left side of the palate was immobile, and the uvula was drawn to the right. Complete aphonia was present. There was relative weakness of the left arm and leg, with normal reflexes. Hypotonicity of the left arm and leg was present. There was complete analgesia on the right half of the body except for the area supplied by the fifth cranial nerve. Crossed anesthesia of the left arm and leg was present. A diagnosis of thrombosis of the posterior inferior cerebellar artery was made. Postmortem examination revealed a fine antemortem clot in the thrombosed left vertebral artery, which extended to the ventral aspect of the medulla where the basilar artery formed.

In this case is revealed a limited distribution of the vertebral artery, for which the collateral circulation at the periphery of the lesion may have accounted. The basilar artery in this case was formed by junction of the two vertebral arteries at the level of the middle of the olive. This emphasizes the importance of anatomic variations in the distribution of the vertebral artery. The presence of the Horner syndrome on the ipsilateral side in sixteen of the twenty-four recorded cases is significant. Apparently, this type of palsy reveals that the central sympathetic pathways do not cross below the level of the pons and, undoubtedly, lie dorsolateral in the medulla, probably close and medial to the spinothalamic tract.

The second case occurred in a man aged 43, single, who on awaking one morning was unable to swallow. He could speak only in a whisper. Difficulty was encountered in standing because of dizziness. He became aware during the course of the day that the right side of his body was numb. During the next twenty-four hours the symptoms abated. Then, when apparently he was convalescing, the left side of the face suddenly became paralyzed and difficulty in swallowing became pronounced. Examination revealed complete aphonia, a blood pressure of 170 systolic and 120 diastolic and enlargement of the heart. Examination of the cranial nerves revealed slight nystagmus on looking toward the right and complete anesthesia and paralysis of the left side of the face. The palate was drawn to the right. The other nerves seemed normal. There were diminution in strength and marked hypotonicity of the limbs on the left side. Complete analgesia of the right side of the body was present, except for an area supplied by the cervical plexus. Impairment of temperature and pain discrimination was evident. Crossed ataxia of the left arm and leg persisted. On the day after admission to the hospital paresis of the left side of the body grew suddenly worse, and he became drowsy. He died twenty-two days after the onset of symptoms. Autopsy revealed thrombosis of both vertebral arteries. Microscopic examination showed a small wedge-

shaped lesion with the base at the periphery and the apex extending inward between the inferior olive ventrally and the spinal nucleus of the fifth nerve dorsally. Accordingly the spinothalamic, rubrospinal and ventral spinocerebellar tracts were completely involved.

Absence of sensory loss over the cervical region on the contralateral side of the body has been reported previously and has been explained by a lesion extending from the periphery inward, thus destroying the superficial and avoiding the deeper fibers of the spinothalamic tract. This explains the absence of sensory involvement in the cervical as well as the thoracic region.

The differential diagnosis of occlusion of the posterior inferior cerebellar artery and that of the vertebral artery is not easy. The diagnosis of involvement of the vertebral artery is probable if the pyramidal tracts are affected.

KRINSKY, Boston.

CEREBELLAR ATAXIC FORM OF HEINE-MEDIN DISEASE. E. GLANZMANN, Schweiz. med. Wchnschr. **67**:972 (Oct. 9) 1937.

Glanzmann reviews the literature on the cerebellar ataxic form of poliomyelitis and describes 2 cases. The onset is generally slow and the patients complain usually of fatigue in the legs and occasionally in the arms. The weakness in the legs becomes so severe that the child is either unable to walk or staggers when attempting to do so. The disorder may take its course without fever or with low fever. As the walk becomes more and more ataxic, the child develops a tendency to fall toward one or the other side. A tendency to fall backward is comparatively rare. Analysis of the ataxia in the author's cases revealed the absence of Romberg's swaying, but in a case reported by Wieland this symptom was present. The finger to nose experiment often fails; in the knee to heel test, the child finds the knee only after long searching, and in aiming movements past pointing with the hand and foot is observed. It is interesting that the signs of meningeal irritation which ordinarily are frequent in poliomyelitis are absent in the cerebellar ataxic form. There is no rigidity of the neck or spinal sign, and even Amoss's sign may be lacking. Kernig's and Lasègue's signs are merely indicated. The four cardinal symptoms for the diagnosis of poliomyelitis fail completely in the cerebellar ataxic form. Of especial interest is the lack of localized paralysis of the extremities. The musculature of the back and of the extremities shows only surprising lack of tonus and more or less pronounced motor weakness. The cutaneous reflexes, particularly the abdominal and the cremasteric, are frequently increased, and the plantar reflexes occasionally. This increase in the cutaneous reflexes seems to indicate irritation in the cerebral reflex arcs. The behavior of the tendon reflexes varies; they may be increased in both extremities or in only one and be reduced or abolished in the other. In the 2 cases reported the patellar and achilles tendon reflexes were abolished. Lumbar puncture reveals slight or no increase in pressure. The spinal fluid is clear; the Pandy reaction is positive and the Nonne reaction usually negative. As regards the clinical course: The author says that complete cure is the usual outcome. That the cerebellar ataxic form is a type of poliomyelitis is proved by the fact that it occurs at the time of epidemics and that transitional forms exist. The author suspects that the process is localized in the brain stem and in the cerebellum.

EDITOR'S ABSTRACT.

Society Transactions

PHILADELPHIA NEUROLOGICAL SOCIETY

J. C. YASKIN, M.D., *President, in the Chair*

Regular Meeting, Feb. 25, 1938

PROGNOSIS FOR ABSCESS OF THE BRAIN. DR. FRANCIS C. GRANT.

Two general principles have been used in the surgical attack on a subcortical abscess of the brain. The difference lies in the size of the opening that is made in the overlying skull. Drainage carried out through a single small burr hole by means of a ventricular puncture needle, with or without the introduction of a small soft rubber drain, may be termed the "closed" method. If the craniotomy is large, e. g., from 3 to 6 cm., and the abscess cavity is opened or excised, with introduction of packing under direct vision, the procedure may be called the "open" method. To reach a conclusion as to the relative merits of the two methods, a series of 31 patients have been observed for over two years. Interest was centered on the physical condition of the patients and the presence or absence of neurologic sequelae in relation to the type of procedure used. The result can best be presented in tabular form.

Method	No. of Patients	Sequelae
Abscess tapped without drainage		
Temporal lobe	1	Hemiparesis persisted
Frontal lobe	2	None
Cerebral region	2	None
Abscess tapped and drained		
Temporal lobe	10	None
	1	Convulsions
	1	Convulsions and death in 7 mo.
	1	Fungating wound; convulsions and death in 9 mo.
Frontal lobe	1	Convulsions and death in 9 mo.
	1	Death from meningitis in 3 yr.
Cerebellar region	3	None
Total number treated by closed method	23	Present in 5 patients
Craniotomy and cortical excision		
Temporal lobe		
Enucleation	1	None
Enucleation	1	Convulsions
Cortical excision	1	Hemiparesis
Frontal lobe	1	None
Cortical excision	1	Convulsions and death in 3 mo.
	1	Convulsions and death in 5 yr.
	1	Convulsions
	1	Meningitis and death in 8 mo.
Total number treated by open method	8	Present in 6 patients

This tabulation seems to indicate that the closed method, with a minimum of cortical damage, gives better final results than does the open procedure. This might have been expected, since in the open attack not only is the cortex incised or excised but cortical herniation with further damage is accepted as a postoperative result.

I have no explanation for the comparatively poor results in cases of abscess of the frontal lobe as compared with those in cases of similar lesions in the temporal lobe. A cerebellar abscess, provided a cure can be obtained, gives few sequelae, owing to the lack of physiologic response from the cerebellum.

DISCUSSION

DR. TEMPLE FAY: The dangers which beset the neurosurgeon in attempting to treat an abscess of the brain are frequently not those he plans for. The lesion may present itself easily or may be difficult to drain or reach. There are many complications, particularly in areas close to the pathways of the cerebrospinal fluid. I do not have a definite plan for dealing with these lesions. I have almost come to the conclusion that decompression over the lesion, permitting herniation of the brain, does something that is favorable in the end. I have seen results when the hernia was treated secondarily which were better than anticipated.

DR. B. J. ALPERS: I have just finished an analysis of 27 cases of abscess of the brain in Dr. Grant's service, with special reference to the formation of a capsule. Is there any correlation between the outcome in cases of abscess of the brain and the formation of a capsule? My experience has been that the older the abscess the more likely the possibility of encapsulation. This is not always true, since abscesses may exist for a long time without encapsulation. An encapsulated abscess, however, does not mean an inactive abscess, since virulent organisms may exist within a well walled-off abscess cavity.

DR. J. C. YASKIN: Dr. Grant did not mention any cases in which the abscess was removed en masse—cases in which the condition had been considered to be tumor of the brain prior to dissection.

DR. F. C. GRANT: I agree with Dr. Alpers and feel certain that statistics for my service show that the longer one waits (with safety) before operating the better the chances; much better results occur with than without encapsulation. Five years ago, my colleagues and I reported 49 cases of abscess of the brain which were divided into two groups—in 30 there was encapsulation, and in 19 there was no capsule. In none of the 19 cases did the patient recover. In the 30 cases in which sufficient time elapsed to permit encapsulation, 20 patients recovered, and 10 died; so the time element is important. I do not think that every abscess of the brain presents a surgical emergency.

HYPERPATHIC AREAS OF THE SCALP ASSOCIATED WITH INTRACRANIAL LESIONS. DR. F. H. LEWY.

Determination of hyperpathic areas of the scalp by dragging a needle over the skin is of assistance in localizing intracranial processes. This is equally true in cases of tumor, abscess, chronic subdural hematoma, arachnitis and meningeal scar formation so far as they are situated above, at or just below the surface of the brain. The correlation between the hyperpathic areas and the locus of the intracranial lesions is close in some cases and approximate in others. A diagram shows the site of hyperpathia in intracranial processes of different localizations. The method is of special value in comatose patients, in the differential diagnosis of supratentorial and infratentorial tumors, in the finer localization of tumors of the cerebellum and sphenoid ridge and in the differentiation of neoplasms and vascular processes.

DISCUSSION

DR. N. C. NORCROSS: McNaughton, of the Montreal Neurological Institute, in a paper which I think has not yet been published, has shown that part of the dura, including the tentorium, is supplied by fibers of the first division of the fifth nerve. I wish to ask Dr. Lewy if this can be correlated with the areas of hyperpathia which he has described.

DR. F. C. GRANT: I can confirm Dr. Lewy's observations. He has worked on material of the clinic; frankly, I was a little skeptical when he initiated this study; now, however, I pay close attention to a hyperpathic zone and find usually that it agrees well with the clinical picture.

DR. B. J. ALPERS: In how many cases is a hyperpathic zone lacking?

DR. TEMPLE FAY: In cases of involvement of the sphenoid wing I can readily understand the reference of pain to the trigeminal pattern. In cases in which the hyperpathic area over the region of the posterior fossa extends from the occipital region to the base of the neck, how is one to explain the reference of pain to this region when it does not agree with the sensory segmental pattern? Such a diffuse pattern resembles one in which pain is referred from the vessels—in this case, the vertebral arteries.

After ligation of the external carotid artery for relief from pain associated with sarcoma of the face, I found that stimulation at the bifurcation of the carotid artery produced pain in the eye, the upper gums, the teeth, the tongue and the temporal area. From the vertebral artery, I have found, pain is referred to the base of the neck, as in the case of the basilar artery.

DR. F. H. LEWY: I am unable to answer Dr. Norcross' question. I have had no personal experience with innervation of the dura. I referred to what is found in textbooks. In reply to Dr. Alpers: The hyperpathic zone is absent in a certain number of cases; I think, therefore, that the importance of the sign as compared with that of other clinical findings should not be overstressed.

Dr. Fay asked a difficult question. I have no direct evidence to show in what way the vascular nerve fibers interfere with the areas of hyperpathia, but I think he is right in stressing the importance of innervation through the vessels. In 1 of my cases, the evidence pointed in this direction. There was a zone of hyperpathia around the temple. The tumor was deep seated, but the middle cerebral artery was completely embedded in it. I explained this deviation from the rule by reference to the vascular innervation. In the case of tumors of the sphenoid ridge the point is different. In 1 case the tumor pressed directly on the second division of the fifth nerve; in the other, on the first. Therefore, in these cases there was a zone which corresponded with the peripheral distribution of the nerve.

ANALYSIS OF THE END RESULTS OF TREATMENT OF 655 PATIENTS WITH TRAUMA TO THE HEAD. DR. MICHAEL M. SCOTT.

In a series of 655 patients with trauma to the head the total mortality was 117, or 17.8 per cent. If the 26 patients who died within the first three hours after admission are excluded, the mortality rate for the group is 13.8 per cent. The distribution according to age decades and the percentage of mortality in each decade shows, as Swift and others have emphasized, that the mortality rate steadily increases with the age but that the total number of patients in each age decade decreases as age advances. In 531 patients there were no complications, such as fractures of the long bones, visceral injuries or meningitis. Of this group 64 died, a mortality rate of 12 per cent. For 124 patients with complications the mortality rate was 42.7 per cent. An operation was performed on only 50 patients; 22 of these died—a mortality rate of 44 per cent for the operative group and of 3.3 per cent for the entire group. The highest mortality occurred in the group with focal signs associated with subarachnoid hemorrhage, which was combined with subdural and epidural bleeding, the mortality rate being 46.6 per cent. For patients with compound depressed fracture or unilateral subdural hematoma, on whom an operation was performed, the mortality rate was 18.7 and 14.2 per cent, respectively. Epidural hemorrhage alone was exceedingly rare, contrary to the usual statement in textbooks; on only 1 patient was operation performed, with fatal outcome.

An analysis of the entire series on the basis of the following clinical groups shows the importance for diagnosis and prognosis of study of the spinal fluid and roentgenographic examination of the skull.

1. Concussion group (no fracture of the skull; clear spinal fluid): 342 patients, with a mortality rate of only 5.5 per cent.

2. Fracture of the skull only; clear spinal fluid: 53 patients, with a mortality rate of 13.2 per cent.

3. Bloody spinal fluid (on at least two punctures); no evidence of fracture in the roentgenograms: 115 patients, with a mortality rate of 26 per cent.

4. Bloody spinal fluid; positive evidence of fracture of the skull: 145 patients, with a mortality rate of 42 per cent.

In 75 per cent of all patients with bloody spinal fluid there was fracture of the skull.

Method of Treatment.—1. The patients were first treated for shock, when present, by the intravenous administration of a 50 per cent solution of dextrose and saline; heat was applied to the body; loss of fluids through sweating was restricted by the use of atropine, and constriction of the vascular bed was effected by hypodermic injection of solution of posterior pituitary and ergot.

2. Lumbar puncture was done after the patient had completely recovered from shock; if subarachnoid bleeding was observed, the canal was drained daily or twice a day until the hemorrhage stopped or the fluid became xanthochromic. This usually occurred by from the fourth to the seventh day.

3. Roentgenograms of the skull were made as soon as the patient's condition was not jeopardized by the procedure.

4. Adequate adjustment of the fluid balance was made. The total fluid intake in twenty-four hours was limited usually to from 20 to 32 ounces (0.59 to 0.94 liters), and a diet low in fluids, salt and carbohydrates was prescribed.

5. Sedation was restricted to the use of sodium bromide, chloral hydrate or phenobarbital by mouth or rectum or hypodermically. Morphine or its derivatives were not used.

6. Methenamine was given in doses of 10 grains (0.65 Gm.) four times a day when there was bleeding or leaking of cerebrospinal fluid from the cavities of the skull.

7. Operation was performed only in cases of compound depressed fracture and in cases in which the neurologic findings and clinical course suggested a focal lesion, such as an epidural, subdural or intracerebral clot.

8. In the average case the patient was out of bed by the fifth or seventh day and was discharged on from the seventh to the tenth day after admission, with instructions to follow the program of restriction of fluids and special diet for at least three months. He was advised to return to his family physician or to the clinic at a specified date for reexamination.

Results of Treatment.—Follow-up studies show that more than 80 per cent of patients who maintained the daily intake of fluid at a level of 32 ounces (0.94 liters) or below were free from the sequelae usually attributed to trauma to the head and were able to return to previous activities within three months.

DISCUSSION

DR. R. H. THOMPSON: I am interested in the statement that recovery from cerebral trauma and discharge from the hospital occurred as early as the seventh day. Recently, on the tenth day after an injury I saw a man who had apparently mild concussion of the brain. He had been kept in bed since the injury; as he had noted no discomfort, he pleaded that he be permitted to return home. Before I had left the hospital, he had a jacksonian seizure, with unconsciousness. At operation a subdural hematoma was discovered.

I maintain that in all cerebral injuries the patient should rest in bed for at least two weeks.

DR. A. M. ORNSTEEN: Dr. Scott stated that of 655 patients with injuries to the head 80 per cent had returned to work in three months. This has not been true in my experience. I am thinking in terms of compensation and liability. I know

patients who received compensation for as long as two years, even though the skull had not been fractured and the cerebrospinal fluid was clear. If one eliminates the changes in personality the question is different. Have the patients who are not receiving compensation been separated from those who are, and have the human and legal elements been taken into consideration?

I allow at least from three to six months' disability in cases of subarachnoid hemorrhage, whether the patient receives compensation or not. If these features are included in the statistics, how can one come to the conclusion that 80 per cent of the patients can return to work in three months?

DR. TEMPLE FAY: Dr. Ornsteen has raised the issue which I wish to discuss. Six years ago, if 40 per cent of patients in my service with cerebral traumatic lesions returned to work within a year my associates and I thought we were lucky. Now, most patients are willing and able to return to work in from six weeks to three months. A careful study is made of each patient, and we assure him that he can recover. He is placed on a strict program of limitation of fluids for three months. He is referred to the family physician or to the follow-up clinic, and the employer is told that he should be able to return to work within three months. The patient must be impressed with the idea that he will recover fully in a certain time. I can give statistics from follow-up studies which show that many patients are made neurotic by lawyers and physicians. It is an indictment against some members of our profession; they talk too much about post-traumatic neurosis and allow the patient to feel that he should be afflicted, even when he is not.

I am sure that of 100 patients with a true post-traumatic condition of any duration about 80 will be able to return to work in approximately three months. I wish to emphasize the importance of restoring proper cerebral circulation and pressure. The brain will work satisfactorily if given sufficient blood and plenty of oxygen. I have treated more than 1,400 such patients. Approximately 9 per cent of persons with organic injuries require a prolonged period of disability and compensation. These patients deserve all that is available for them; the others are capable and will return to work. My attitude is that if the patients do not deserve compensation they will not receive it; my reports will not help them. I am of the opinion that the "post-traumatic neurosis," with its many vague and hypothetic causes can be avoided. More time is spent by patients trying to prove that they were unjustly injured than in trying to recover. They should be put to work.

DR. A. M. ORNSTEEN: When Dr. Fay discharges patients from the clinic he sends them back to the family physician. I do not know how much contact he has with them after discharge. After the family physician has treated them for a time they come to me! I have seen patients with severe injuries to the brain back at work in four weeks, but some patients with a slight contusion stay out for four or five years. The case goes to court; the experts testify that there is a post-traumatic neurosis, and the insurance company pays. It is not the oxygen or the lack of oxygen in the brain that causes the trouble; it is the ideas that physicians put into the patients' heads!

DR. B. J. ALPERS: The charts which Dr. Scott showed seemed to indicate that subarachnoid hemorrhage is associated with a mortality of 23 per cent. This is at variance with my experience in cases of cranial trauma. I have found that subarachnoid hemorrhage, whether with or without fracture, is usually benign, provided no extensive cerebral laceration or contusion has occurred. Has not Dr. Scott included with the patients with subarachnoid hemorrhage a number with something more than pure subarachnoid hemorrhage? Are there not in this group a number of patients with cerebral damage as well?

DR. J. C. YASKIN: It is of interest that in the whole series there was only 1 patient with hemorrhage of the middle meningeal artery. I am not clear whether Dr. Fay, in his discussion, differentiated between the postconcussion syndrome

and the post-traumatic neurosis. Does he mean to imply that he can restore 80 per cent of either of these types of patients to work in a short time, even when litigation and compensation are involved? Is not the management of these two conditions entirely different?

DR. MICHAEL SCOTT: In reply to Dr. Thompson's statement about the rate of recovery following injury: I agree with him that it depends on the clinical course. Patients are not discharged from the hospital until they are comfortable and free from headache or other complications that demand continued hospital care. I agree with Dr. Alpers that when there is bloody spinal fluid there must have been laceration of the brain; otherwise, there would be no bleeding into the subarachnoid space. In Dr. Fay's clinic we are sure that the finding of blood in the fluid is not due to technical error since whenever this type of fluid is encountered puncture is made daily or twice a day until the bleeding stops, usually by from the fourth to the seventh day after the injury. Since bloody spinal fluid is a sign of cerebral injury, its diagnostic and prognostic significance is obvious, especially since it is accompanied by a marked rise in the mortality rate.

STATISTICS ON 1,061 PATIENTS ON WHOM ENCEPHALOGRAPHIC AND VENTRICULOGRAPHIC STUDIES WERE MADE. DR. JOHN H. TAEFFNER.

Not infrequently, the neurologist and the neurosurgeon, in order to weigh the advantages and disadvantages of diagnostic pneumocranium in a given case, need to consider the risk associated with the procedure. With this in view, the records were reviewed of 972 patients at the Temple University Hospital on whom encephalographic and 89 patients on whom ventriculographic studies were made. Except for patients with block in the posterior fossa or with high intracranial pressure, encephalographic examination was the method of preference because of the greater amount of information derived and the relative simplicity of the procedure. In patients with tumor of the posterior fossa on whom encephalographic study was made, the procedure, although usually well borne, did not give adequate information because of failure of the ventricular system to contain air or because complete drainage was not risked; there is, however, not a sufficient number of these cases to warrant analysis.

The part played in the death of the patient by the procedure adopted is open to relatively wide interpretation. The complete records of all patients who died within four weeks after an injection of air were reviewed. The records of those who died within two weeks were carefully studied, even though operative procedures may have intervened. This was done because a craniotomy undertaken as an emergency to combat a condition evidently induced by injection of air does not transfer the responsibility for the fatality. Otherwise, a subsequent craniotomy or an injection of air would take precedence, so to speak. Any death within three days after the injection of air, regardless of the preoperative condition, was considered to be due to the injection of air.

The 1,061 persons were unselected and included the general run of patients in a neurologic and neurosurgical service requiring pneumocranium for study. The injection was made in 168 patients with tumor of the brain or with the diagnosis of suspected tumor of the brain at the time of discharge.

For 3 of the 972 patients with encephalographic, and 10 of the patients with ventriculographic, examination the results were fatal, the mortality rates for the encephalographic and the ventriculographic procedures being 0.3 and 11 per cent, respectively. The mortality resulting from the encephalographic method was due to hemorrhage: A man aged 55 with hypertensive encephalopathy experienced subarachnoid hemorrhage a few hours after an encephalogram was made and died in three days; a man aged 49 with arteriosclerosis had an intracerebral hemorrhage shortly after encephalographic examination and died in four days; a man aged 43 had a hemorrhage into a tumor of the parietal lobe. Craniotomy performed as an emergency was futile, and he died in less than twenty-four hours.

Four of the fatalities after ventriculographic examination occurred in patients whose operative and postoperative condition was described as good. Three had pathologic lesions in the posterior fossa (2 tumors, and 1 syphilitic meningitis). Death resulted from relatively sudden respiratory failure in ten, twenty and thirty hours, respectively. One patient with a cerebellar tumor, whose preoperative condition was fair, had respiratory difficulties shortly after the exchange of air was begun. She responded fairly well at first, but died in eighteen hours.

The other 6 patients were in poor condition before the procedure: The pathologic condition in each case was a space-taking lesion in some part of the brain; 2 patients died before leaving the operating room; 3 others died within the first twelve hours, and 1 reacted fairly well to the procedure but died within forty-eight hours. These 6 deaths can be attributed to the ventricular injection of air only for the purpose of this study; the patients presented very poor risks originally; inclusion of their cases raises the mortality rate from 4.5 to 11 per cent. The other fatalities all occurred in conditions in which injection of air by the spinal route is considered to be contraindicated, raising the question of the feasibility of employing the encephalographic method in such cases.

Since February 1934, the date of the last death following encephalographic examination, more discrimination has been used in selecting arteriosclerotic or hypertensive patients for such studies; coincidentally, no fatalities from this examination have been encountered in the last four years.

DISCUSSION

DR. W. DUANE JR.: In the group of patients with tumor which Dr. Taeffner has mentioned was the intracranial pressure increased?

It has been my belief that it is not advisable to make encephalographic examination when there is an increase in intracranial pressure. It seems to me that in some of the cases reported by Dr. Taeffner death was due to medullary herniation following the introduction of air and removal of fluid by lumbar puncture.

As yet, I have been fortunate in not having had a death after encephalographic study, but this is due, I believe, to the fact that I seldom perform this procedure when there is marked hypertension or increased intracranial pressure. For patients with increased intracranial pressure I prefer the ventriculographic method.

DR. F. C. GRANT: Dr. Fay and I have been fighting since 1926 over the question of the relative mortality rates of the encephalographic and the ventriculographic procedure. I do not understand why Dr. Fay should have anything like a mortality rate of 11 per cent from the ventriculographic method. This is not true in my cases; it may be because an operation is performed immediately. It may not be possible to introduce enough air into the ventricles, but one certainly obtains some indication of the trouble. One can always make a decompression on that side. This, of course, may not seem an adequate explanation for a mortality rate from the ventriculographic procedure which I am sure is not over 2 or 3 per cent, since the patient is not subjected to the diagnostic procedure. After all, what is attempted by ventriculographic examination is the localization of a tumor so that it can be removed at once. That is why Dandy reported 500 cases in which there were no deaths. If one localizes a tumor by ventriculographic or encephalographic examination, one is grossly negligent if the tumor is not removed as soon as possible. In the last four or five years I do not think that I have seen a patient in whom, as a result of the manipulation necessary for the ventriculographic procedure, a relatively satisfactory preoperative condition changed to one in which I believed operation would be hazardous.

DR. W. E. CHAMBERLAIN: At this clinic it is emphasized that one must operate immediately. The patient is usually on his way to the operating room; so I do not think that a delay in operation is a factor. I think that others of my associates in the roentgenographic department will agree that we are urged to

speed. The point is that the mortality from ventriculographic studies at the Temple University Hospital would be far less if more were made, because it would change the statistical balance.

DR. TEMPLE FAY: I think that Dr. Grant and I see this problem from different angles. I understand his point of view. In 2 cases of this series an operation might have been performed immediately, but was not; perhaps this was an error in judgment. In 6 cases there was no question of delay.

Dr. Grant may recall, when we were working together, that the ventricular needle once passed through the internal capsule and in another instance penetrated a tumor. I have had several horrible experiences that have made me cautious in using the ventriculographic procedure. I should not have a ventriculographic study of my brain if some other means would prove as satisfactory. Ventriculograms, however, must be made in cases of lesions of the posterior fossa. I think now that it is safer to make an encephalogram instead of a ventriculogram in cases of tumor above the tentorium. Dr. Duane is to be congratulated that he has not had a fatality as a result of encephalographic studies.

I think that both procedures are necessary adjuncts to diagnosis and should be used as complementary measures. One method should never be used when the other is indicated or is safer, merely because of personal preference on the part of the operator.

DR. J. C. YASKIN: It is my opinion that a neurosurgeon would be benefited by more frequent consultation with a neurologist regarding the advisability of air studies. In my experience, encephalographic study is never performed when there are evidences of increased intracranial pressure, as manifested by papilledema, increased intraspinal pressure and deformation of the sella turcica or other roentgenographic evidences. In the presence of increased intracranial pressure I always advise against taking an encephalogram and insist on ventricular studies if air studies are indispensable.

MYELOGRAPHIC DEMONSTRATION WITH AIR OF HERNIATIONS OF THE NUCLEUS PULPOSUS OR CARTILAGINOUS DISK. DR. BARTON R. YOUNG and DR. MICHAEL SCOTT.

The posterior protrusion of a cartilaginous disk is readily demonstrated by roentgenograms made after the subarachnoid injection of air, especially if the lesion is in the lumbar region. The encroachment on the subarachnoid space by the herniated disk produces a defect in the air column, which may be visualized in either or both of the anteroposterior or the lateral projections. Ordinarily, the ventral limiting membrane of the subarachnoid space is sharply delineated in lateral roentgenograms, but if the intervertebral disk is displaced dorsally a posterior displacement or bulge is noted. It is essential that the fluid in the lumbocaudal sac be completely replaced by air, with the patient in the Trendelenburg position, or interpretation of the roentgenograms will be difficult. The accuracy of myelographic examination with air as a diagnostic procedure is attested by the fact that in each of 35 cases in which operation was performed the exact level of the lesion demonstrated by air was confirmed at operation. In 10 of these cases there was a herniated disk. In 6 of the 10 cases the lesion was in the lumbar region; in 3, in the dorsal region, and in 1, in the cervical region of the spine.

DISCUSSION

DR. W. E. CHAMBERLAIN: The chief advantage of using air is that one dares to use it in many cases. Iodized poppyseed oil was not used until the diagnosis was almost clinched. It seems that air could be used in cases in which the diagnosis is not cut and dried. I think that that is the chief advantage of air.

UNUSUAL COMPLICATION FOLLOWING SUBOCCIPITAL CRANIECTOMY. DR. ROBERT A. GROFF and DR. MELVIN W. THORNER.

A patient on whom suboccipital craniectomy had been performed experienced fleeting pain in the back and abdomen four months after the operation, and finally over both legs. Examination revealed zones of hypalgesia to pinprick over the regions in which there was complaint of "spontaneous" pain. These areas corresponded to the first and third lumbar nerves bilaterally. Roentgenograms of the spine disclosed two silver clips, one opposite the first lumbar root and the other opposite the third. After sedation and rest the hypalgesic areas disappeared, and the patient has remained free from symptoms for the past five months.

Migration of silver clips in the cranial subarachnoid space is not rare. The wonder is not that it occurs but that it does not occur more often. The unusual feature in this case was the extent of the migration, which was the greatest that has been observed in the clinic with 1 exception; in that case the clip caused no symptoms.

DISCUSSION

DR. F. C. GRANT: Dr. Groff started this study recently. I imagine he will find that in 100 cases there are 10 or 12 in which a clip in the lumbar sac has caused no symptoms; that is, if the patient is not informed about it.

SYRINGOMYELIA AND MULTIPLE SCLEROSIS SIMULATED BY DEFORMITIES IN THE UPPER CERVICAL REGION OF THE VERTEBRAL CANAL. DR. W. E. CHAMBERLAIN.

Experience indicates that in no other part of the vertebral canal are neurologically significant deformities so apt to be overlooked as in the upper cervical region. Both neurologically and roentgenologically, the evidence may be baffling and interpretation be fraught with special difficulties.

REPORT OF CASES

CASE 1.—In the case of E. F., a white man aged 20, a hopeless prognosis had been given for a condition which had definitely been diagnosed as "syringomyelia, high in the cervical region" after thorough study in two reputable neurosurgical clinics. On more than one occasion roentgen studies of the cervical portion of the spine had been pronounced "negative" or "without clinical significance." Had the history not suggested the possibility of a traumatic etiologic factor, I might not have made the thorough roentgenographic studies which resulted in a diagnosis.

The earliest symptoms (paresthesias and slight limitation of motion in the cervical portion of the spine) appeared immediately after a slight, but unusual, accident. The patient, at the age of 17, slipped while carrying a heavy canoe on his head, supported by a "tonk strap." Subsequently he played on the college football team and suffered several severe injuries, two or three of which resulted in unconsciousness. The symptoms and signs became characteristic of syringomyelia.

Exhaustive roentgenographic study revealed that the floor of the posterior fossa of the skull was molded as though from being pressed upward into the cranial cavity. The cervical vertebrae were closer to the cranial vault than normal. Accompanying this "telescoping" of the cervical portion of the spine into the posterior fossa of the skull were telescoping of the vertebral parts and narrowing of the upper cervical portion of the spinal canal.

Doubt was cast on the diagnosis of "significant stenosis of the upper cervical part of the spinal canal" by the fact that some roentgenographic findings pointed toward a congenital anomaly in this region. Operation by Dr. Temple Fay not only demonstrated constriction of the cord at the site of stenosis of the canal but produced marked and rapid clinical improvement through mechanical removal of the stenosis.

CASE 2.—L. T., a white woman aged 28, had an illness which was diagnosed as "multiple sclerosis," not as a final desperate attempt to classify an undetermined condition but through demonstration of a characteristic neurologic picture. In spite of a record of normal roentgenographic findings, a careful roentgenologic study was made because the patient gave a history of having been thrown from a horse and falling on her head. A malunited fracture of the base of the odontoid process of the second cervical vertebra, with definite encroachment on the spinal cord, was seen.

Operation by Dr. Temple Fay disclosed local pressure on the spinal cord; enlargement and reconstruction of the spinal canal were followed by rapid clinical improvement.

DISCUSSION

DR. TEMPLE FAY: In both the cases which Dr. Chamberlain has described the condition was considered at times as multiple sclerosis. In 1, mild syringomyelic manifestations had been present for a time. The diagnosis of syringomyelia, multiple sclerosis and degeneration of the cord was made by three prominent neurologists. Neurologic studies in my clinic indicated a lesion in the region of the second cervical segment, in spite of the intrinsic involvement of the hands. Dr. Chamberlain found this lesion after taking more than 50 roentgenograms for measurement. In both instances the patient recovered after relief from compression of the upper cervical portion of the cord.

I think that Dr. Chamberlain has made a real contribution in this regard; it is important to recognize that extradural compression and disturbance of circulation of the cord may simulate a diffuse intrinsic disease.

VALUE OF PERCUSSION OF THE SKULL IN LOCALIZATION OF GROSS CEREBRAL LESIONS. DR. AUGUSTUS MCCRAVEY.

For several years my associates and I have been using percussion of the skull in the neurosurgical department of the Temple University Hospital. When the bell of the stethoscope is placed on the forehead and the scalp is struck with the finger, or better with a rubber hammer, certain characteristic changes in pitch and note are traceable to gross cerebral lesions.

Characteristic changes in percussion note have been observed after cerebral vascular accidents, and Dr. Fay has pointed out these changes in cases of accumulations of fluid and cystic localizations. The note for the hydrocephalic skull is characteristic, and the typical changes in note heard on percussion over an endothelioma, a subdural and an epidural hematoma, an abscess of the brain and a solid glial tumor situated near the surface are unmistakable, although extremely difficult to describe. Authorities, such as Dr. A. C. Morgan and Dr. C. L. Brown, have been unable to give an appropriate description of the various pathologic sounds developed by percussion over intracranial lesions.

When a change in percussion note is associated with tenderness in a definite area there is almost certain evidence of an underlying lesion, and this lesion may even be beneath the surface of the brain. The examiner can recognize the normal changes in percussion note which occur over the temporal muscle, the vault and the base of the skull and also the influence of the thickness of the hair and scalp on the note evolved.

REPORT OF CASE

A child aged 4 was admitted to the Temple University Hospital with the history of a furuncle of the right external auditory canal, followed by headache and vomiting. The optic disks were choked bilaterally, with swelling of 1 diopter; no focal neurologic signs were discovered. There was definite change in the percussion note, with persistent tenderness over the left frontoparietal area. Encephalographic examination showed obliteration of the left lateral ventricle; exploration revealed a large, encapsulated subdural abscess compressing the entire left cerebral hemisphere.

We have found this method of localization confirmed repeatedly at operation. The procedure has become a routine in Dr. Fay's service at the Temple University Hospital, and we consider that it is reliable in approximately 75 per cent of the cases.

DISCUSSION

DR. F. C. GRANT: In confirmation of Dr. McCravey's observations: Three or four years ago, Drs. Davis and Haven elaborated a machine with which an electrical percussion hammer produced a sound. This was demonstrated at a meeting of the Neurosurgical Society with the idea that it would be valuable. I think Dr. McCravey's suggestion has the advantage of simplicity. One does not need an electrophysicist to keep the apparatus going, and it seems that this method is just as valuable. Davis and Haven, as far as I know, have not reported any results. I am a little skeptical, for that reason, of the value of percussion sounds. The percussion method for discovering tenderness is generally satisfactory. I am not convinced of any other particular value.

DR. TEMPLE FAY: Dr. Harold Palmer will recall that in 1928 we used an electrocardiographic machine at the Philadelphia General Hospital for percussing the head. The waves produced with the machine varied with the thickness of the hair and the temporal muscles. We were unable to find enough bald-headed men with whom to experiment and so gave up this method. Dr. McCravey did not describe the present sound-recording apparatus, with which it sounds when a single tap of the finger on the skull is amplified as though one were trying to exterminate the patient.

The test is not infallible, but the neurosurgeon will find a high degree of correlation and verification at operation. A tumor, a clot, edema and even a thrombotic lesion each has a characteristic sound.

J. C. YASKIN, M.D., *President, in the Chair*

March 25, 1938

EFFECTS OF ACUTE ANEMIA ON NERVE ACTIVITY. DRS. D. W. BRONK, M. G. LARRABEE (by invitation) and J. B. GAYLOR (by invitation).

The influence of decreased circulation on nerve activity was investigated by stimulating the preganglionic nerve to a sympathetic ganglion while recording the impulses discharged from the ganglion cells over the postganglionic fibers. It is also possible to record impulses in fibers which have come through the ganglion without synapse and thus to compare the effects of anemia on axons and on synaptic regions.

In the case of the stellate ganglion of the cat, we observed the following significant facts:

1. From five to ten minutes after arrest of circulation certain units failed to conduct. All failed within from thirty to fifty minutes.

2. Through pathways lose their power to conduct in about the same length of time as do those with synapse. One must conclude, therefore, that some axons are no more resistant to anemia than are some synapses and nerve cells.

3. Postganglionic cells can be stimulated directly by perfusion with acetylcholine. When conduction through the ganglion fails because of circulatory arrest the cells can no longer be stimulated by acetylcholine. It therefore follows that the postganglionic cell fails as soon as, if not sooner than, the presynaptic terminations and the transmitting mechanism.

4. In acute anemia, the basic structure of nerve tissue maintains its state of organization long after it loses the capacity to conduct impulses. This is shown by the fact that the ganglion regains its power to conduct impulses when the circulation is established after seven and a half hours, during which time conduction was completely blocked.

MODIFICATION OF SPONTANEOUS CORTICAL ACTIVITY BY SENSORY STIMULI. DRS. F. H. LEWY and G. D. GAMMON.

The cortex of the cat under anesthesia induced with pentobarbital sodium exhibits bursts of rhythmic activity at irregular intervals. Our aim in this study was to determine whether this activity is dependent on the normal sensory inflow. Since we were interested in the response of the cortex as a whole rather than that of the primary sensory areas, leads were taken from the suprasylvian gyrus, behind the sensory area. The waxing and waning rhythm could be abolished by section of the brain stem at the level of the colliculi, by destruction of the optic thalamus or by interruption of thalamocortical fibers in the internal capsule. Progressive diminution of the bursts occurred when successive cuts were made through the spinal cord, the medulla and the pons. On the other hand, removal of the cerebellum, the opposite hemisphere, both occipital or both frontal lobes did not abolish the rhythm. These observations thus suggest that the spontaneous rhythm is dependent in some way on the integrity of the normal sensory pathways. This dependence is more marked with anesthesia induced with pentobarbital sodium than without anesthesia, which is in confirmation of Bremer's experiments. Even in the unanesthetized cortex, however, the pattern is profoundly altered.

To determine how sensory stimulation alters the spontaneous cortical activity, sensory nerves, the thalamus and the thalamocortical fibers were stimulated. By this means bursts of activity could be driven by repetitive single shocks, the bursts usually escaping from the drive after several minutes. Long inhibition usually followed stimulation. If the cortex showed no activity the stimuli aroused a waxing and waning rhythm, lasting several minutes; if activity was minimal the amplitude and frequency could be increased.

These two lines of evidence support the concept that the spontaneous activity of the cortex is modified by impulses which constantly flow into the brain from the body. This effect is apparent not only in the primary sensory areas but in other parts of the cortex, and possibly in the cortex as a whole.

DISCUSSION ON PAPERS BY DRS. BRONK, LARRABEE AND GAYLOR AND LEWY AND GAMMON

DR. G. P. MCCOUCH: I had no intention of discussing these papers, but I cannot let pass the opportunity in the first paper—of expressing my amazement at the rule which was clearly demonstrated—that a nerve fiber will fail virtually as quickly as a synaptic region. That, to me, is a completely revolutionary concept. That finding is one of the most remarkable in neurophysiology of which I know.

DR. J. C. YASKIN: I wish to ask Dr. Bronk how he reconciles his findings with those of several years ago which demonstrated the danger of anoxemia in various portions of the nervous system. I think that for practicing neurologists this may be of extreme interest.

DR. D. W. BRONK: I shall make two observations in reply to Dr. Yaskin's question. When experimental neurologists have compared the rapid failure of the central nervous system deprived of its circulation with that of the peripheral nerves, they have stimulated the peripheral axons only infrequently. There are now abundant grounds for assuming that the cerebral cortex is always fairly active. One should therefore compare its rate of failure during anemia with that of a nerve deprived of its circulation which is conducting impulses at a fairly high frequency. When this is done, the differences in the time of failure are not as

great as one has generally believed. Even then, however, peripheral nerves will survive longer, and this difference must probably be considered as due to a difference in the rates of metabolism.

RELATION OF POTASSIUM TO FAMILY PERIODIC PARALYSIS. DR. G. D. GAMMON.

A summary of this paper appeared in the *Proceedings of the Society for Experimental Biology and Medicine* (**38**:922, 1938).

INFLUENCE OF CHEMICAL AGENTS ON PROPERTIES OF NERVE TISSUE: A. MODES OF ACTIVITY OF PERIPHERAL AXONS. DRS. F. BRINK JR. (by invitation), J. SJOSTRAND (by invitation) and D. W. BRONK.

The importance of the chemical content of the fluid which bathes a nerve in regulating its irritable properties and modes of activity is discussed and illustrated by the results of recent experiments on chemical stimulation of single nerve fibers. The idea is stressed that these environmental changes merely bring about the conditions under which modes of activity inherent in the fundamental molecular organization of the nerve tissue may manifest themselves. This point of view is discussed in relation to possible localized chemical changes giving rise to the syndromes associated with certain types of malfunction of the nervous system.

In particular, the various types of rhythmic activity observed in nerve fibers the Ca^{++} ion content of which has been lowered are discussed. The additive stimulatory effect of anoxia and of a low Ca^{++} ion content is illustrated. Finally, the stimulatory and the subsequent inhibitory effect of K^{+} ions on nerves the Ca^{++} ion content of which had been lowered is analyzed.

INFLUENCE OF CHEMICAL AGENTS ON PROPERTIES OF NERVE TISSUE: B. EFFECTS OF ARTERIAL BLOCK ON THE HUMAN ULNAR NERVE. DRS. MELVIN W. THORNER and F. BRINK JR. (by invitation).

An experimental study is presented in which the irritability of the ulnar nerve in situ was observed during a period of oxygen deprivation. A characteristic cycle of changes in irritability was found. This cycle agrees well with the results obtained with excised nerve. The cycle of irritability is fairly constant for a normal, healthy person. In patients with peripheral neuropathies the alterations from the normal in the cycle of irritability furnished a sensitive and dependable index of the clinical progression or retrogression of symptoms and was thus of consequence in the evaluation of various types of therapy.

INFLUENCE OF CHEMICAL AGENTS ON PROPERTIES OF NERVE TISSUE: C. FUNCTIONAL PROPERTIES OF HUMAN NERVES AND THEIR DEPENDENCE ON THE CHEMICAL ENVIRONMENT. DRS. R. S. WIGTON and F. BRINK JR. (by invitation).

A study of the functional properties of the peripheral nerves in 5 patients with hypoparathyroidism is presented. The patients were followed during a period of control when calcium and viosterol were given, during a period when therapy was withdrawn and tetany developed and during the administration of dihydrotachesterol (a 0.5 per cent solution in oil), which restored the former calcium level of the blood.

The nerve function studied was that of accommodation, measured by the response of the nerve to slowly rising currents. The power of accommodation fell and rose in a characteristic fashion with corresponding parallel changes in the value of the blood calcium. By this index it was found that the functional state of the peripheral nerve can be determined in a quantitative fashion, and more accurately and consistently than with the use of the usual signs and symptoms employed. As an electrical test of nerve function in man, the method has certain significant advantages over the usual methods employed.

The dependence of the functional properties of the peripheral nerves on the calcium balance in the blood is graphically illustrated by a quantitative measure.

DISCUSSION ON PAPERS BY DRS. BRINK, SJOSTRAND AND BRONK, THORNER AND BRINK AND WIGTON AND BRINK

DR. D. W. BRONK: I believe that these investigations indicate a useful means of studying fluctuations in the chemical composition of the blood. Nerve tissue is extremely sensitive to changes in its ionic environment, so that measurements of its electrical irritability and time constants should provide a delicate and sensitive index of the state of the body fluids. Such studies of the properties of peripheral nerve tissue should also be invaluable in providing a clue to the chemical influences to which the cells of the central nervous system are subjected.

PHILADELPHIA PSYCHIATRIC SOCIETY

BALDWIN L. KEYES, M.D., *President, in the Chair*

Regular Meeting, April 8, 1938

SO-CALLED GRAPELIKE DEGENERATION IN BRAIN TISSUE. DR. A. E. TAFT, Bryn Mawr, Pa.

A condition seen in fixed and stained brain tissue was described more than twelve years ago as grapelike degeneration. The name characterizes the morphologic pattern. It was first considered peculiar to dementia praecox, but this idea was abandoned when it was observed in other conditions. In the literature, including textbooks, it is stated that the lesion is made up of multilocular cysts and that mucin is associated with the condition. These descriptions are somewhat confusing, since two distinct processes are concerned. The condition is not a degeneration. The common factor is edema of the brain. With suitable illumination it can be seen that the so-called cysts contain crystalline material. There are usually also small globular bodies embedded in the tissue, which are said to stain like mucin. With the dark field they appear to be precipitated protein. Both appear only in the white substance. That both occur postmortem and are due to the effect of fixatives is indicated by the fact that they are seen with great frequency along the cut border of the section. The explanation for both these appearances may well be that the substances in the brain fluid, which are known to be altered in edema, have been precipitated by the fixing fluids. The question of mucin is not without interest clinically, since work already reported in the literature indicates that increase of mucin in the blood stream depresses the central nervous system.

DISCUSSION

DR. HELENA A. RIGGS: This study is important for the light it throws on one of the worst stumbling blocks in neuropathology—the significance of artefacts and postmortem changes. The so-called artefacts and postmortem changes in the brain are not present in all specimens submitted to the same type of fixation and fixed at the same time after death. In the same specimen not all areas are similarly affected. In the case of specimens in which there are obvious morphopathologic changes to explain the clinical findings, one is prone to dismiss the structures that Dr. Taft has described as of no significance. More and more, however, one is confronted with cases in which there is clinical evidence of disordered neural function but no categoric structural change except that usually cataloged as "postmortem degeneration." In these cases one is faced with the dilemma either of admitting that neural function may be altered without changing the structure of the tissue or of reevaluating the alterations in brain tissue which have previously been dismissed as of no significance.

In pathology, interpretation of visceral disease rests no longer solely on morphologic change of structure but on evaluation of the abnormal physiologic state which has caused such a change. Thus, what formerly was considered as postmortem autolysis of the adrenal medulla assumes important functional significance in the light of Cannon's studies on the sympatheticoadrenal mechanism. The experimental work of Cushing, D'Amour and others has forced alteration of concepts of the pathologic change in the stomach which was once pigeonholed as postmortem digestion of the fundus.

In a similar manner, Dr. Taft's work has demonstrated that while grapelike degeneration is a postmortem artefact, it can occur only when there has been antemortem alteration in the physiologicochemical makeup of the brain. It is only when profound and acute alterations of the barrier between the blood and the brain occur, as evidenced by acute cerebral edema, that one may expect to find these artefacts in the fixed and stained sections of the brain. These artefacts are observed so consistently in certain types of conditions that one feels justified in giving a general description of the clinical and pathologic picture in a theoretic case in which one might expect these changes to be present.

The patient is acutely ill with delirium, coma or convulsions. There is frequently severe hyperpyrexia, without evidence of infection. The blood pressure may be elevated above the normal for this person, and the pulse and respiratory rates are increased. The patient is thirsty, but the output of urine is scant; urinalysis may show albumin and sugar, although previously renal function was known to be normal. The red cell count is normal or high, in spite of clinical evidence of moderate anemia, but estimation of the viscosity of the blood demonstrates that this is due to concentration. The clinical course is short—usually a few days, rarely more than two weeks. The mortality is alarmingly high. Post mortem no organic changes are observed that can account for death, but all organs show intense acute passive congestion. The changes in the viscera have been completely described and evaluated by Dr. Virgil Moon, under the descriptive term "acute medical shock."

The brain presents the same picture of acute edema, but here the skull limits free expansion, so that the brain stem is crowded through the foramen magnum and circulation in the vital centers is interfered with. The immediate cause of death is asphyxia of the vital centers of the medulla, but the edema of the brain has the same etiologic basis as that of the visceral organs.

This is the type of case in which one may predict, with reasonable accuracy, the presence of Buscaino's grapelike degeneration, but there is no disease entity for which it is pathognomonic. I have observed this type of degeneration in acutely edematous brains in such widely diverse clinical conditions as diabetic acidosis, insulin shock, hyperemesis gravidarum, heat stroke and trauma to the head.

Dr. John G. Reinhold: The apparent association of the grapelike "degeneration" with the smaller blood vessels of the brain suggests that the abnormality may be humoral in origin. It is well known that chemical changes in blood affect the brain. Dehydration with deficiency in sodium chloride is accompanied by cellular edema. If severe and protracted, dehydration leads to failure of blood supply and local asphyxia. Excess of electrolytes in the extracellular fluid likewise is injurious. Anoxia is a highly important potential source of injury to the brain. Not only is the brain susceptible to lack of oxygen in a metabolic sense but anoxia leads to increased permeability of the capillaries, with escape of plasma colloids into the tissue. The cells of the brain, ordinarily bathed in fluid practically free from protein, thus become exposed to direct contact with these substances, so that the cell environment is radically changed. Equilibria between the electrolytes and fluids are altered. Cell membranes are exposed to the action of plasma proteins and lipoids. Abundant evidence is available showing that these substances alter the permeability of cells.

Photomicrographs shown by Dr. Taft support her suggestion that several types of this condition exist. The most plausible explanation is supplied by the

observation of Dr. Riggs that conditions associated with change in the barrier between the blood and the brain predispose to appearance of this abnormality. Any of the factors mentioned, as well as many others, may bring about such an alteration.

PSYCHIATRIC OUTPATIENTS WITH A SINGLE INTERVIEW. DR. LAUREN H. SMITH and DR. REYNOLD A. JENSEN, Boston (by invitation).

The Institute of the Pennsylvania Hospital, which started to function in 1930, is interested primarily in the diagnosis and treatment of the psychoneuroses. In addition, it offers a consultation as well as a psychologic and vocational guidance service to the city of Philadelphia and the surrounding territory. It is hoped that from a study of its patients will grow an appreciation and understanding of the forces and factors which produce maladjustment in the lives of so many persons. In this sense, it endeavors to serve as a center for the promotion of a program of mental hygiene. While its work is divided into two departments, the inpatient and the outpatient, the latter is considered to represent its more vital function in relation to the community at large.

During the first six years of the institute's existence over 1,600 patients were seen in the outpatient department. Many of these had only one contact with the institute. This paper is a report of an analysis of 386 cases in which but "one contact" was made, i. e., in which the patient visited the institute only once. He may have been seen by the psychiatrist or the psychologist or both, but these interviews were held during the same visit to the institute.

This study determined the distribution according to age and sex, the source of referral, the marital, economic and educational status, where the patient lived, the diagnostic impressions, the disposition made, the number who refused help, the number who were unsuitable for psychotherapy and the number who were given additional appointments but failed to return.

The distribution of the two sexes was about equal. Distribution according to age preserved a fairly regular curve for the adults, with the greatest number of patients falling between the ages of 21 and 40. The majority of patients were referred by agencies or medical sources, many coming from physicians in private practice. Relatively few were referred by family or friends, and few came of their own accord.

The usual reason for referral from medical sources was consultation and treatment, while from agencies the request was, in the main, for psychiatric or psychologic opinions and recommendations. The reason for referral from other sources was usually treatment. The majority of the patients lived in Philadelphia or the immediate vicinity, and others, in outlying small towns and the country. There was almost equal distribution between patients who were married and those who were unmarried, patients under 16 being left out of account. The greater number had poor economic status, and relatively few, good. A large number were unemployed at the time of contact with the institute. Many others were attending schools or doing domestic or unskilled labor. Relatively few were skilled workers or professional persons.

Diagnostically, it was thought that 88 patients were definitely psychotic and 107 neurotic. Fourteen were thought to have either severe neuroses or early psychoses, and 27 were suffering from some organic disturbance or residual complications of organic disease. The disturbances of the rest of the patients were divided among alcoholic, speech, sexual, behavioral and psychologic problems. A few patients were considered as average persons.

Of the 386 patients, 227 were not acceptable to the institute for treatment, and other plans were formulated for them. Sixteen refused further contact, having come in under duress, while 11 felt that they were sufficiently helped by one interview to carry on by themselves. No record of disposition was given for 28 patients. Ninety-nine patients were given appointments, but did not return.

The paper discusses the consultation and psychologic service rendered the community, as well as possible reasons for the patients' failure to return for subsequent interviews. The necessity for adequate preparation of the patient and the importance of the first interview in a psychiatric case are considered.

PROPOSED CLASSIFICATION OF PSYCHIATRIC PROBLEMS. DR. GEORGE S. SPRAGUE, White Plains, N. Y. (by invitation).

There is need of a type of classification which will permit workers in various fields of psychiatry to compare the problems encountered and results achieved by means of a common terminology and which also, in the teaching of medical students, will aid in explaining the provinces of psychiatry. A scheme of eight headings to meet these needs is proposed:

1. Problems of intellectual level
2. Problems of school placement and adjustment
3. Problems of special capacities, interests and disabilities
4. Problems of personality and emotional adjustments
5. Problems of objectives, ideals, beliefs, unenlightenment, etc.
6. Problems of social and recreational adjustment
7. Problems of psychosis
8. Problems of physical pathology

The use and some of the advantages of the classification are described.

DISCUSSION

DR. ARTHUR P. NOYES: Dr. Sprague's paper is stimulating and presents a classification which from many points of view is more desirable than any hitherto employed. One may think of mental disorders from three points of view. The first is that of the present official classification, which approaches disorders of personality as if they were definite disease entities. This is exceedingly unsatisfactory in that it tells one practically nothing concerning the individual patient. It, of course, makes possible certain statistics, which undoubtedly have value. For the clinical psychiatrist, however, who is interested in the patient rather than statistical classifications, it is disappointing. The second point of view is the genetic-dynamic one. This is of great value in helping one to understand how the patient has been subjected to various physiologic or psychologic stresses and has come to behave in the way which is described as a mental disorder. Dr. Sprague's classification or point of view is, however, more comprehensive, since a scheme which is based on the patient's problem must include the genetic-dynamic factors and, as has been stated, leads directly to the subject of therapy. It would be more helpful if one were to think of patients in terms of problems.

Dr. Sprague's group of problems, which he characterizes as one of objective or purpose, contains much that is suggestive in the field of psychopathology. Since doubtless much in the life of the average person is determined by problems which are included in Dr. Sprague's classificatory scheme, it is one to which much thought could be given. It is in the sphere of problems he has mentioned that the so-called normal and diseased personalities frequently touch.

DR. J. C. YASKIN: Dr. Sprague's presentation is a natural outgrowth of the traditions of psychiatry in New York State. Commencing with the early works of Adolf Meyer, followed by the studies on personality by Hoch, Amsden, Kirby and others, the neurologic group has contributed a great deal to the understanding of the prepsychotic personality and the factors leading to psychoses. In his present presentation, Dr. Sprague attempts to correlate the earlier work with psychiatric problems in everyday practice.

There can be little disagreement as to the value of his presentation. He subdivides the subject matter into four sections, which deal successively with problems related to intellectual functions, emotional activity, behavior patterns

and physical situations. There can be no doubt that the scheme he has elaborated is useful for both diagnostic and therapeutic purposes. It is natural for the group in Philadelphia to think that the physical situation should receive a more conspicuous place in the scheme, although they are fully aware that a great many psychotic conditions are influenced little, or not at all, by physical changes.

CHICAGO NEUROLOGICAL SOCIETY

MEYER SOLOMON, M.D., *President, in the Chair*

Regular Meeting, March 17, 1938

COMPARISON OF PSYCHOLOGIC "REPRESSION" AND NEUROLOGIC "INHIBITION." DR. ROY R. GRINKER.

Comparison of repression and inhibition, which are basic principles in psychoanalysis and neurology, respectively, indicates that the two concepts are dynamically identical. These terms include two dynamic factors: (1) the abandonment of a figurative level of activity, which is the negative aspect, and (2) the adoption of a new level of activity, which is the positive aspect. The direction of the dynamic alteration varies in development, disease and learning.

This paper will be published in full in the *Journal of Nervous and Mental Diseases.*

ANTIDOTAL TREATMENT OF BARBITURATE INTOXICATION: REPORT OF TREATMENT WITH PICROTOXIN IN SIX CASES. DR. W. J. BLECKWENN and DR. MABEL G. MASTEN, Madison, Wis.

This article was published in full in *The Journal of the American Medical Association,* Aug. 6, 1938.

The use of picrotoxin as an antidote in barbiturate poisoning had its inception in the experimental work on animals by Tatum and his associates (*J. Pharmacol. & Exper. Therap.* **41**:465 [April] 1931; **44**:337 [March] 1932). Tatum and we (*J. Pharmacol. & Exper. Therap.* **60**:99, 1937) presented clinical experimental work before the American Society for Pharmacology and Experimental Therapeutics, in April 1937, in which the technic of the administration of picrotoxin was developed in treatment of patients narcotized with known doses of shorter acting barbiturates. From this work it was discovered that 1 mg. of picrotoxin acts as an antidote for approximately from 30 to 40 mg. of pentobarbital sodium, sodium amytal or their thioderivative.

Six cases of poisoning due to a self-administered barbiturate (sodium amytal was most commonly employed), taken with suicidal intent, in 5 of which picrotoxin was used with success, are reviewed.

We urge physicians to be alert to the recognition of barbiturate poisoning in patients in coma presenting small fixed pupils, corneal anesthesia, low blood pressure, shallow respiration, fast weak pulse and varying degrees of cyanosis. We emphasize that effective treatment consists of the following measures: gastric lavage and purgation; continuous administration of oxygen; intravenous injection of picrotoxin in a 1:1,000 solution, at the rate of 1 cc. per minute until the return of pupillary and corneal reflexes; diuresis by parenteral administration of fluids and repeated intravenous injections of 100 cc. of 50 per cent sucrose to combat edema, and injection of dextrose to prevent acidosis. When emergency treatment is delayed and symptoms may be due largely to cerebral edema, dehydration and administration of oxygen are considered highly important.

DISCUSSION

DR. HENRY BROSIN: During the past few months there have been 2 cases at the Billings Hospital which loosely parallel those which Dr. Masten has cited in the amount of drug ingested, the method of treatment and the amount of picrotoxin administered. One case was that of a man aged 23, with schizophrenia, who took 24 capsules of barbital, 5 grains (0.324 Gm.) each, at 7 p. m. to escape hallucinations. He was discovered the next day at about 3 p. m. and brought to the hospital, where emergency treatment was given. Picrotoxin was given in the manner described between 4 and 7 p. m.; there were occasional return of some of the reflexes and gradual periods of recession until about midnight, when he appeared to be safe from immediate danger. When admitted, he was in a state of shock, with a temperature of 104 F.; he was given blood transfusion, dextrose, caffeine, epinephrine and 25 per cent solution of pyridine betacarbonic acid diethylamine (coramine). The next day he was sluggish, but out of danger. After forty-eight hours, the temperature began to rise, owing to lobar pneumonia in the left lung, from which recovery was uneventful. Unfortunately, the experience did not affect the schizophrenia.

DR. RICHARD KOHN: I have had the opportunity to treat 5 patients with picrotoxin; 4 of them recovered, and I was therefore especially interested in this paper. I wish to bring out one point. I found in the literature a fine survey by Gillespie, who said that in many cases it is not possible to ascertain how much drug the patient has taken. According to Dr. Masten, the amount of the drug taken is not a deciding factor in the final outcome. I may mention 1 case described in the literature: A patient who had taken 130 grains (8.45 Gm.) of barbital was treated with moderate doses of caffeine with sodium benzoate U. S. P. and recovered. A woman aged 64, whom I saw about twenty hours after she had taken 90 grains (5.85 Gm.) of barbital, was in a state of cerebral and pulmonary edema. She was given about 80 mg. of picrotoxin and died in a few hours. Another patient, who had taken an unknown amount of phenobarbital, was seen three days later, when there was pulmonary edema. Treatment with picrotoxin was continued for three days; 672 mg. was given, and the patient recovered, after a second attack of pulmonary edema had been counteracted by solution of posterior pituitary and strophanthin. There finally developed an abscess of the lung, from which the patient also recovered.

I wish to point out the difference between the effect of long acting and that of short acting drugs. The latter have a much more depressing action on the respiration. A young woman took an unknown amount of pentobarbital sodium; eight hours later, when I saw her, she was in a Drinker respirator. I started treatment with picrotoxin; she was removed from the respirator after 12 mg. of picrotoxin had been given, and she recovered within a few hours. I believe in pushing picrotoxin, in fractional doses, because it gives the patient a chance to react. With from eight to ten minutes as the interval, injections are given in doses indicated by the previous reaction—as an average, from 6 to 12 mg. One patient, after the administration of 70 mg., showed only one slight attack of convulsions of the arms and head. The treatment was resumed about thirty minutes later. I think the treatment should be pushed until not only the corneal reflexes are normal but the patient keeps on moving, because this prevents stasis. If this is done, there is also less danger of aspiration, which may result in abscess of the lung. I think Dr. Masten and I have obtained the same results with somewhat different technics.

DR. JULES MASSERMAN: I wish to ask if, in the patients who have taken so great an amount of the drug, there is not permanent damage of the central nervous system after apparent recovery. The work of van der Horst and the Keesers indicates that this may be so. As to the administration of sucrose: That seems to be an ideal agent not only for reduction of cerebral edema but for production of marked diuresis. However, the solution must be used in amounts of from 100 to 300 cc. in 50 per cent concentration, because amounts less than that have been found to be ineffective in man.

DR. ROY GRINKER: Dr. Masten called attention to the laxity of the laws in this country, which enables patients to secure barbiturates without a prescription. She might also have indicated the ease with which neurologists are inclined to write prescriptions which enable patients to take large quantities of these drugs.

I wish to stress that it is not only the acute effect of the drug that is dangerous. Several years ago, Tatum and Seevers produced chronic artificial poisoning in dogs and sent the brains to me for study; there was no question that chronic ingestion produces serious damage to the brain. There were many hemorrhages, particularly in the white matter; the ganglion cells showed a toxic effect, and there were changes in the glia, indicative of the toxic effect on the parenchyma. In the literature many cases are reported in which there were similar changes in the deep structures, particularly in the region about the ventricles; so it is not only the danger of acute barbiturate poisoning for which one must take responsibility in prescribing for a patient but the fact that habitual use may produce changes in the brain.

DR. DAVID SLIGHT: I think it is interesting, with respect to the neuropathologic effects of barbital poisoning, to recall that a study of this problem in dogs was one of the last pieces of work reported by Sir Frederick Mott before his death, about fourteen years ago. I had been led to believe that this work was repeated by others and disproved.

DR. MABEL MASTEN: It seems that sodium amytal is more popular in Madison, while barbital is the barbiturate of choice in Chicago. It is gratifying to hear of the success which Dr. Brosin and Dr. Kohn have had in the use of picrotoxin as an antidote in poisoning due to one of the longer acting barbiturates. Dr. Brosin commented on the high temperature with which his patient came to the hospital, thinking that this circumstance necessitated certain emergency measures. Fever was a symptom common to all our patients. This is the result not of infection but probably of disturbance of the heat centers.

Dr. Slight is interested in knowing whether there are permanent mental alterations as the result of prolonged cerebral anoxia. We have not followed any of these patients beyond their immediate recovery from the intoxication, except for the university senior student who took 156 grains (10.11 Gm.) of sodium amytal and was in coma five days. She had decided that life was unbearable, for many reasons. One was her inability to determine on a career for herself. The slow healing of the trophic ulcer required a long period of hospital care. She acquired an interest in hospital service and is at present taking the university course for laboratory technicians. She is very happy in this arrangement. Perhaps the result of prolonged cerebral anoxia may be compared with the alterations induced by prefrontal lobotomy, which is being promoted in this country by Dr. Walter Freeman.

Not more than 100 cc. of sucrose was given at one time, although this was repeated frequently. Good diuresis was obtained, and it was assumed that resolution of cerebral edema was being effected in the presence of continued diuresis. It was often possible to obtain 600 cc. of urine by catheterization two or three hours after the administration of fluids and sucrose.

ROLE OF THE ENDOCRINE GLANDS IN MENTAL DISORDERS. DR. HUGH T. CARMICHAEL.

A critical review of the major arguments advanced for and against the theory that the endocrine glands play an important etiologic role in mental disorders is presented. Special consideration is given to the examination and evaluation of the claims made by supporters of the theory. These claims include: (1) reports of a high incidence in persons with mental disorders of constitutional anomalies of types common in endocrine dysfunction, with the suggestion that there may be a constitutional endocrine deficiency; (2) observations post mortem of histopathologic changes in the glands of internal secretion of psychotic patients; (3) reports of various metabolic deviations in patients with mental illness; (4) claims of

beneficial effects from administration of glandular extracts and hormones; (5) deviations in behavior observed in disorders of some of the endocrine glands, e. g., the mental deficiency in cretinism and the apparent slowing of the mental processes in myxedema; (6) claims of changes in the hormone levels of the blood and in the hormone excretion in the urine, and (7) the association of certain mental disorders with periods such as puberty and the climacterium, in which there is known to be a disturbance in endocrine balance. A detailed description of the literature is not offered, nor are the individual endocrine glands or the individual mental disorders considered as such. The survey is restricted to the clinical evidence in man. Illustrations from my experience are given. Caution is urged against too ready acceptance of apparently successful results of treatment with endocrine preparations, and the necessity for establishment of strict criteria in the use of endocrine therapy in mental disorders is pointed out. The quasiquantitative nature of present methods of hormone assay is emphasized.

It is concluded that while there is no crucial evidence against the concept of a close relation between the endocrine glands and mental disorders, there is no definite evidence for it; that until proof is presented it is premature to make vague generalizations about the importance of the glands of internal secretion in mental disorders, and that the actual significance of the hormones in these disorders is still a problem for research.

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DISCUSSION

DR. ALLAN T. KENYON: I have been much interested in the reaction to testosterone propionate bearing on one phase of this problem. It appears that one can secure the expected increase in secondary sex characteristics in men with hypogonadism with proper doses of this androgen. With this, there occurs an increase in erections and in sexual excitability. This reaction in one of my patients was so intense that the patient was much aroused, with priapism and an inclination toward women which he had not felt for a long time. Although much remains to be done, the androgenic substance at present appears to have a powerful influence on the nervous system.

DR. HUGH T. CARMICHAEL: I wish to thank Dr. Kenyon for his discussion, particularly for having mentioned what perhaps the majority have not realized—that is, the probability that one can help persons afflicted with impotence, which in the majority of instances is due to psychic influences.

LOCALIZATION OF CEREBRAL CORTICAL LESIONS BY ELECTROENCEPHALOGRAPHIC EXAMINATION. DR. THEODORE J. CASE.

In a surprisingly high percentage of cases, my colleagues and I have been able to localize lesions of the cerebrum, particularly tumors, by alterations in the electroencephalogram. The advantages of the clinical application of the method are obvious. Unlike the clinical manifestations of cerebral disease, the electrical changes which accompany lesions in the so-called silent areas are as definite and localizable as those arising from lesions in any other portion of the cerebral cortex. The method is simple of application, once the apparatus has been set up. The examination does not require the attention or the active cooperation of the patient. It is not a tiring or painful experience. No anesthetic and no surgical procedure is necessary. It in no way endangers the patient's life or disturbs his physical condition. The records are graphic, objective and impersonal. Any method with such advantages, which offers information of positive value in the diagnosis and localization of cerebral lesions, as does this, is a valuable adjunct to the diagnostic armamentarium of the neurologist.

Tumors and certain other lesions usually give rise to slow waves, and sometimes to spikes, which undoubtedly arise from the disturbed tissue around the tumor. These electrical phenomena may be sharply localized, and by them the position of the tumor may often be well determined. Most of the waves which

are obtained about tumors, and which might well all be classified as delta waves, range in frequency from about 0.5 to 4.5 or 5 per second, the most common frequency being 1 or 2 per second.

A series of 11 cases—8 cases of cerebral tumors of various types, 2 of traumatic cerebral scars and 1 of marked localized scarring of the meninges—is reported. In all, the pathologic condition was determined either at operation or at autopsy or was demonstrated by pneumoencephalographic examination. The location of the pathologic lesion and the approximate localization as indicated by the electroencephalograms were in substantial agreement. Various alterations in the spontaneous electrical discharge limited to the region of the lesion were obtained. These alterations consisted of five phenomena: (1) waves at a frequency of from 0.5 to 3 per second, which were the most common; (2) slow shifts of potential occurring from once in five to once in two seconds; (3) sharp spikes; (4) electrical discharges characteristic of localized convulsive seizures, often without any other manifestations of the seizure, and (5) absence of the normal alpha rhythm.

Waves having frequencies of from 0.5 to 3 per second, which are sensibly equidistant from peak to peak for at least 5 cycles, seem to be characteristic of tumors, but are also seen with other localized pathologic lesions. Except for waves occurring at a rate of 3 per second, commonly seen with minor epilepsy but not as distinctly localized or lateralized as with tumors, such waves when obtained from patients while awake have always indicated gross cerebral pathologic changes.

Great care must be exercised in the interpretation of the various signs. This is particularly true of the spikes; an occasional isolated spike carries little weight, but when seen in considerable numbers or in series they seem to imply a cortical discharge.

It is perhaps unnecessary to emphasize that these waves, especially those with a frequency of from 0.5 to 3 per second, come in trains or spindles and that their amplitude varies from time to time. Because of this, multiple simultaneous recording from several areas of the head is essential to any certainty of localization. It is believed that the electroencephalographic method, while it is of necessity somewhat indefinite in outlining cerebral tumors and lesions, compares favorably in this regard with many of the methods now in use and that there are many lesions which it is possible to indicate more or less definitely by this means when other methods give only normal findings. In view of these possibilities it is likely that the electroencephalographic procedure will become an essential adjunct in the localization of intracranial lesions.

DISCUSSION

Dr. A. Earl Walker, New Haven, Conn.: I have been interested in following Dr. Case's work in the localization of cerebral lesions. One frequently is consulted by patients, 20, 30 or 40 years of age, because of generalized epileptic attacks, perhaps two or three, occurring for the first time in adult life. Many of these patients have no evidence of a focal neurologic lesion. Yet in from 10 to 15 per cent, the convulsion is the first manifestation of a cerebral tumor (Walker, A. E.: Convulsive Seizures in Adult Life, *Arch. Int. Med.* **58**:250-268 [Aug.] 1936), and in a smaller percentage, of cerebral scarring, both of which may be treated surgically. In a certain number it is possible by the electroencephalographic method to show a focal lesion of the cortex, and hence to make early the diagnosis of an intracranial expanding lesion or a scar. Knowing by the use of this innocuous and simple procedure that such a lesion probably is present, one is encouraged to employ the more difficult and unpleasant method of air injection to determine the nature of the lesion. By the use of the electroencephalographic method it may be possible in the future to spare the greater percentage of persons suffering from convulsive attacks occurring for the first time in adult life the misery of encephalographic examination. The electroencephalographic procedure is therefore a particularly welcome adjunct to diagnosis of the convulsive states occurring primarily in adult life.

DR. PERCIVAL BAILEY: Dr. Case has not a great number of cases of focal cortical lesions due to other conditions; so although he states that these waves are characteristic of tumors, I think one is correct in pointing out that he has examined more patients with tumors than other lesions.

DR. RICHARD B. RICHTER: From the data collected, what weight, if any, can be put on the absence of abnormal findings in the electroencephalogram?

DR. JACOB KASANIN: In what way does Dr. Case differentiate between an electroencephalogram in a case of an expanding lesion with convulsions and one in a case of epilepsy of idiopathic character?

DR. THEODORE J. CASE: There are many cases in which it is not possible by this means to say whether a lesion is present or not; in other words, the findings are negative, as in many other examinations. This may arise from several causes. These waves come and go, and it may be that the examination is made at a time when the patient does not show any waves, or there may not be waves which arise as the result of a lesion; the lesion may not cause pressure.

Dr. Bailey is correct; we have been particularly interested in, and have examined many, patients with reference to tumors. I suspect that the number in whom tumor was discovered was 16 or 17, whereas the total number of patients examined was more than 200.

As I mentioned before, it is impossible to say from a normal, perfectly smooth tracing that a patient does not have epilepsy or that he does not have a tumor, although I think the chance of missing epilepsy is much greater than that of missing a tumor.

It is sometimes difficult to tell idiopathic epilepsy by this means. There seem to be two types of idiopathic epilepsy: a type having a large, generalized increase in electrical activity in all parts of the brain and a type in which the record appears normal. The type with a large generalized increase of activity is, I think one can say without question, idiopathic. Other kinds are not so readily diagnosed by this method. An expanding lesion does not produce this generalized increase in activity, but usually gives rise to delta waves.

NEW YORK NEUROLOGICAL SOCIETY

MOSES KESCHNER, M.D., *President, in the Chair*

Regular Meeting, April 5, 1938

DIFFICULTY IN SPELLING AND CEREBRAL DOMINANCE. DR. MARK KANZER (by invitation).

Difficulties in spelling frequently occur in cases of functional and organic disease of the brain. They may result from a general intellectual defect or from a specific disability, such as aphasia or strephosymbolia. The supposition that a special type of spelling difficulty is associated with functional disturbances of the dominant cerebral hemisphere receives support from the following case.

A school girl aged 14 had a history of generalized convulsive seizures for two years; there were neural signs suggestive of diffuse degenerative disease of the brain. An encephalogram revealed moderate internal hydrocephalus, but no evidence of a focal lesion. In the last few months the patient had shown intellectual defects, among which difficulties in spelling were outstanding. Analysis of the mistakes in spelling revealed that they consisted chiefly in a tendency to invert the order of letters. Thus "chicken" might be spelled "chikcen"; "house," "hosue," etc. Further investigation showed that although these errors occurred both in oral spelling and in writing with the right hand, they were not present in the written product of the left hand. A similar tendency to confuse certain words,

such as "there" and "their"; "which" and "witch"; "quit," "quite" and "quiet," was demonstrated in right-handed script, but never occurred when the left hand was used. The patient revised the order of numbers in an address or in a date, but could write them promptly and correctly with the left hand. On occasions when she wrote simultaneously with both hands, errors in spelling occurred on the right but not on the left. However, efforts at simultaneous writing sometimes resulted in twitching of the arms and attacks of petit mal. Reversals of the order of syllables and phrases also appeared.

The general intelligence of the patient was average for a child of her age, but subnormal in performances requiring visuokinesthetic activity. There was no finger agnosia, no disorientation for left and right and no difficulty in reading or simple arithmetic. Aphasic disturbances of an amnesic type sometimes occurred. With practice, the patient learned to spell many words correctly. She was always aware of her errors after she had made them, but could offer no explanation for the mistakes. There was no facility in mirror writing and no confusion in regard to individual letters.

Inquiries revealed an early disposition to left handedness, which had been overcome by training. The patient was still left eyed. There was a history of emotional disturbances which had begun five years earlier, with the birth of a younger sister. The patient had repeatedly shown jealousy of the younger sibling, had run away from home twice and had made a suicidal attempt at least once. The emotional disturbances had become intensified since the onset of the present illness.

The intellectual disturbances displayed by the patient were considered from organic, functional and psychogenic aspects. Disclosure of a definite pattern showing reversals in the automatic reproduction of visual and auditory symbols was regarded as evidence of a functional disorder akin to the reversals in automatic behavior found in association with organic lesions of the brain and resembling the "undoing mechanisms" of psychogenic origin. The occurrence of similar phenomena in aphasia and in cases in which left-handed children have been trained to use the right hand indicates that these disturbances result from disruption of the functional organization of the brain in respect to dominant and subjugate hemispheres. The suggestion is made that, as a result of the diffuse organic disease of the brain, the artificially developed dominance of the left hemisphere produced disintegration and regressive disturbances which account for the disability in spelling and other disorders reported in this case.

DISCUSSION

DR. PAUL SCHILDER: This is indeed a fascinating observation. As far as I know, there is no other instance in the literature in which the spelling with one hand was different from that with the other. I shall start the discussion with the problem of dominance. It is interesting that Dr. Kanzer has cited the famous case of Liepmann (Das Krankheitsbild der Apraxie, *Monatschr. f. Psychiat. u. Neurol.* **8**:15, 1900; Drei Aufsätze aus dem Apraxiegebeit, Berlin, S. Karger, 1905; Apraxie, *Ergebnisse der Medizin von Brugsch,* Berlin, Urban & Schwarzenberg, 1920, vol. 1, p. 516) in which there was apraxia of the right hand. Liepmann stated that this symptom was due to a lesion of the fiber tracts of the left supramarginal gyrus. Today, one assumes that apraxia is due to a lesion not of the connecting tracts but of a center in the left supramarginal gyrus. In a later communication, Liepmann noted that the function of the left hand was also impaired to a lesser extent. If the left center does not function correctly, the centers of the right hemisphere show impairment of function. One is dealing with "sympathic" apraxia (Liepmann) of the left extremity. This is based on the dominance of the lest hemisphere with regard to motility patterns. When the dominant left center is destroyed or cannot send its impulses through the corpus callosum to the right center, the left hand assumes a lower level of function; the left hand becomes awkward. Parts of the left hemisphere are necessary to permit the fully developed function of the

left hand. A similar mechanism was present in this case. Here the right hemisphere was dominant. Only when the right hemisphere was dominant and the patient was writing with the left hand were normal writing and spelling achieved. When, however, the left hemisphere was dominant and the patient was writing with the right hand, the brain was functioning on a lower level. This case is an excellent instance of normal, though faulty, dominance. The disturbance was not an apraxic phenomenon in the right hand but difficulty in spelling on the right when the dominant (right) hemisphere was not in full action. This was the unique feature of the case.

One generally speaks of reversals when single letters or the sequences of letters are reversed; "b" may be changed to "d" and vice versa, and "was" into "saw." This is a change in orientation of left and right and may be called a true reversal. However, one should distinguish reversals of this type from changes in sequence, which have a more general connotation. A change in the sequence of sounds and letters takes place in speech disturbances in cases of dementia paralytica. Similar changes also take place in cases of motor aphasia. One has no right to speak of reversals in such cases. The patient changes the sequence of letters (sounds) without merely reversing from left to right, or vice versa. Dominance consists not only of preservation of orientation for left and right but of maintenance of the correct sequence in speech, reading and writing. One should go one step further in studying dominance. Not only correct sequence but the entire orientation in space is altered by a lesion in the dominant hemisphere; likewise, orientation with regard not only to left and right but to below and above and before and behind is changed. Correct spatial orientation is possible only when the dominant hemisphere is functioning correctly. This is shown by the fact that when defective function produces disturbances in form figures are turned not only 90 but sometimes 180 degrees. One finds also complete turning upside down. In normal cerebral function, sequences in speech, writing and spelling are properly achieved, and forms are placed in space in correct relation with regard to left and right, below and above and before and behind. In the present case one must reckon also with disturbances in form which were not due alone to sequence and reversals. There were other word changes—the word "witch" became "which." In this more primitive type of function, one encounters alterations, reversals, changes in sequence and, finally, additions and subtractions of single letters. All these primitive functions appear in writing only when the dominant right hemisphere is submerged and the inferior left hemisphere is in power.

I think that such disturbances can result from comparatively localized lesions; in this case, there were indications of widespread lesions. There were disturbances in speech, form and spelling. Exact localization is not possible.

What is the relationship between the psychologic and the organic factors in these cases? I think one should distinguish between the different types of psychologic reactions associated with organic disease of the brain. One must remember that symptoms due to organic disease of the brain show the same physiologic and psychologic features in their finer mechanisms as symptoms of general psychologic disorders. Condensations, additions, subtractions and changes in sequence occur in dreams. Psychologic mechanisms found by psychoanalysis are the same as psychologic mechanisms found in cases of organic disease of the brain. Furthermore, every psychologic change associated with organic disease has its reverberation in consciousness. In a case of reading disability, the person does not want to read. I should call the feeling of strain and stress the immediate reflection of the organic disturbance in consciousness. This provokes a psychologic reaction of a compensatory type. One finds, for instance, that these persons acquire an enormous interest in mechanical things. Finally, the compensatory reactions of a psychologic nature in the case of organic disease are directly related to the general pattern of the personality. The child with reading disability who has been pushed in reading and has had no outlet in work and mechanical occupation will become obstinate.

DR. ISRAEL STRAUSS: After the discharge of this child from the hospital, Dr. Kanzer gave instructions as to her treatment; when she returned for further study Dr. Kanzer found that she had improved a great deal under training and that it was sometimes difficult to have some of the errors produced. One day I presented her before a clinic; under the emotional stress of the occasion she showed a great many of the abnormalities which had to a certain extent been covered up by the training. An interesting feature in this case, which I should like to hear commented on by Dr. Schilder, is this: When the patient attempted to write with both hands it was evident that she was placed under a tremendous strain. She did not look at all at the writing with the left hand. She concentrated entirely on the right hand, while the left hand acted almost automatically and gave a perfect result. Once or twice under these conditions she had an attack of petit mal. At one time in this experiment a generalized convulsion was precipitated. To me, it is an interesting psychologic phenomenon that, with the patient under tension, it was possible to bring about either petit mal or a general convulsion.

DR. PAUL SCHILDER: The facts mentioned by Dr. Strauss are interesting from a general point of view. Again, all psychologic mechanisms have organic consequences. One can see this better in a case of organic than in one of psychogenic disturbance. I wish all those who doubt the validity of the psychophysiologic mechanisms discovered by psychoanalysis would study closely a patient with aphasia or agnosia; they would soon be convinced.

DR. GEORGE H. HYSLOP: Dr. Kanzer may be interested in hearing of an interesting and unusual anatomic substrate for specific disabilities in reading and writing. The youngster was first brought to me when he was 4 years of age. He came of right-handed stock on both sides. When his mother had been pregnant about two months she had a severe illness. Embryologically, it was the period when there may be lag or displacement in the development of the neural tube. At birth the child had agenesis of the motor cranial nerves on the right, from the trigeminal nerve down. He also had a lesser degree of agenesis of the right cervical segments, affecting the shoulder girdle and muscles of the upper extremity. At the age of 5 years he was tested for abnormalities in cerebral dominance; eyedness and footedness were found to be right sided. When the child entered school there developed specific disabilities in reading and writing. He has been submitted to training procedures in the last few months, including measures designed not only for the correction of specific difficulties in reading and writing but for improvement of function of the upper extremities, such as archery, swimming and bowling.

I have wondered whether the language problems dealt with in the various specific disabilities in reading, spelling and writing in the individual person are in any way connected with differences in language groups. In Pitkin's book entitled "The History of Human Stupidity," mention is made of an African tribe whose language is agglutinative and so clumsy that abstract words are practically impossible to devise. The vocabulary of this group is necessarily extremely limited. In listening to Dr. Schilder's remarks, I noticed several times that the order of his words was characteristic of the person trained in German. Dr. Schilder at times showed complete reversal of entire words as compared with the order in English. The order of words in Latin and Greek is of interest in this regard. Chinese and Hebrew may be called sinistrad languages.

DR. MARK KANZER: I am glad that Dr. Strauss brought up the emotional factor, which obviously colored the patient's difficulties in spelling. There is no question that when she was emotionally upset the normal automatic course of her spelling was influenced and errors occurred more frequently. This agrees well with Dr. Schilder's observations that the character and personality of the patient enter into these difficulties.

DISTURBANCES OF THE OPTIC NERVE COMPLICATING DISEASE OF THE ACCESSORY NASAL SINUSES. DR. ISRAEL STRAUSS and DR. WILLIAM NEEDLES.

Rhinologists and ophthalmologists differ widely in their estimation of the frequency of disorders of the optic nerve complicating sinusitis. The neurologist must concern himself with the problem, even though certain aspects lie outside his domain, because multiple sclerosis, as well as other neurologic entities, comes up for consideration in differential diagnosis in these cases.

In cases of rhinogenic involvement of the optic nerve, the disease usually begins with fairly sudden diminution of vision. This is generally unilateral, less often bilateral. Not infrequently there is an accompanying infection of the upper respiratory tract. Periorbital pain, tenderness on pressure over the eyeballs and pain on movement of the eyeballs are common symptoms. In typical cases a central scotoma exists. Van der Hoeve said that enlargement of the blind spot is characteristic of retrobulbar neuritis. The pathologic process may confine itself to the retrobulbar portion of the nerve, so that the fundus appears normal. If the process is situated more anteriorly and involves the nerve head, optic neuritis results. The sinuses generally held responsible are the sphenoid and the ethmoid. Frank suppuration in the sinuses is rare.

Seventeen cases were studied in this series. The first group was composed of cases in which a relation between disease of the sinuses and that of the optic nerve appeared fairly definite. In the instances in which eradication of the suspected focus of infection could be carried out prompt improvement in the visual status resulted.

Another group was composed of cases in which the relation between disease of the sinuses and that of the optic nerve was still in doubt, even after painstaking investigation.

A third group consisted of cases in which the diagnosis of multiple sclerosis had seriously to be considered. In multiple sclerosis, retrobulbar neuritis may be the first signal of the disease and may precede the appearance of other symptoms by a decade or more. In rare cases the papilla may be involved, and a picture indistinguishable from papilledema may occur. If the typical signs of disseminated disease of the nervous system are present, the diagnosis is apparent. However, one must not lose sight of the fact that a patient with multiple sclerosis may have sinusitis and, secondary to it, retrobulbar or optic neuritis. Whether multiple sclerosis may render the optic nerve more vulnerable to involvement from an infected sinus or, conversely, whether an infected sinus may predispose the optic nerve to disease by the process of multiple sclerosis must remain speculative.

Finally, a case is described in which the most apt designation for the condition appeared to be "sphenoiditic hydrocephalus." The bilateral papilledema was ascribed to increase in intracranial pressure secondary to disease of the sphenoid sinuses. Sinusectomy was followed by improvement.

In the differential diagnosis of diseases of the optic nerve resulting from disease of the sinuses the following conditions must be considered: multiple sclerosis, Leber's hereditary optic atrophy, cerebral neoplasms in the vicinity of the optic nerve, syphilis, toxic retrobulbar neuritis and various infectious diseases which occasionally result in retrobulbar neuritis.

Roentgenologic study of the optic foramen, as suggested by White and Goalwin, may throw light on the pathogenesis of rhinogenic retrobulbar and optic neuritis, but as yet the findings are inconclusive.

Certain objections put forth by investigators, such as von Hippel, who deny a rhinogenic origin for diseases of the optic nerve do not seem to us to stand careful scrutiny. As a result of the study of our cases, as well as of those reported by other observers, we have formulated certain conclusions. Although we are mindful of the frequency of multiple sclerosis as a cause of retrobulbar neuritis and of the large percentage of patients with retrobulbar neuritis who spontaneously recover, as well as of the patients who are reported to be cured after simple adrenalization of the nose, though we realize that disease of the sinuses

is present in such a large proportion of the population that it may erroneously be incriminated as the cause of a host of conditions and though we recognize also the occasional untoward effects of surgical procedures on the nose, it is, nonetheless, our opinion that in some cases operative intervention is indicated. We do not go to the extreme, advocated by some, of insisting on histologic examination of tissue before dismissing the sinuses as normal. If, however, the specially trained rhinologist concludes, as a result of examination, that the sinuses are diseased and if no other cause of the neuritis is apparent, we favor eradication of the focus, especially if continued observation shows progression in visual impairment. It may be that a number of our patients would have shown improvement spontaneously and that the disease of some will eventually prove to be multiple sclerosis. No one can be certain, however, that in others, if left untreated, permanent atrophy of the optic nerve would not have developed. Who, so long as such a possibility exists, will be content to wait a decade or more on the chance of the final appearance of multiple sclerosis rather than take immediate remedial measures? A healthy reaction from indiscriminate surgical treatment of the nose should not lead one to the other extreme of withholding such treatment when it is urgently indicated—especially since, in competent hands, untoward effects are rare. Even in cases in which the diagnosis of multiple sclerosis is well established, if retrobulbar or optic neuritis is present and diseased sinuses, which may be the responsible factor, are present, we think treatment of the sinuses as if multiple sclerosis did not exist is justified.

DISCUSSION

DR. KAUFMAN SCHLIVEK: It is important to separate the cases into those of optic and those of retrobulbar neuritis. The paper groups these under one heading. Moreover, the cases of unilateral and those of bilateral involvement should be differentiated. In 4 of this series of cases of unilateral involvement optic neuritis was due to disease of the sinuses and was much improved after operation. Two were cases of atrophy of the optic nerve of long standing, and, naturally, the condition was not helped by operation. In 1 case there were multiple sclerosis and sinusitis, and it is questionable whether the operation had any effect. In 1 there was retrobulbar neuritis due to disease of the sinuses and operation did not help.

Of the cases of bilateral involvement and sinusitis definite improvement was shown in 1, but no follow-up study was made. In another case there was some improvement, and later vision was reported to be poor; no follow-up study was available. I should say that it is difficult to make inferences concerning the results obtained by operation on the sinuses in any of the cases of bilateral involvement reported, unless one excepts the last case.

Ophthalmologists are generally agreed that optic neuritis is frequently due to disease of the nasal sinuses, and operation is advised, particularly if the condition is unilateral. Retrobulbar neuritis, however, is usually not of rhinogenic origin. In by far the greater number of cases, the disease is due to multiple sclerosis, but if vision continues bad operative procedure is advisable. In these cases the good effect is possibly due to hemorrhage or bloodletting. However, there is no doubt that in some cases retrobulbar neuritis is definitely due to sinal disease. A combination of multiple sclerosis and disease of the sinuses is also possible. I think one should be particularly careful in cases of bilateral optic neuritis, particularly bilateral papilledema. In these cases Dr. Needles overemphasizes the rhinogenic origin. Even if in such a case there is evidence of sinusitis, both clinically and roentgenologically, the condition should be given the last etiologic consideration. Many patients have had numerous operations on the sinuses and later the condition has proved to be due to other causes; not infrequently, valuable time has been lost.

DR. RUDOLPH KRAMER: There is much discussion between ophthalmologists and rhinologists as to the effect disease of the nasal sinuses has on the optic nerve. The rhinologist will say that the correlation is frequent. A reason is that he

sees patients who have been weeded out by the ophthalmologist and the neurologist; they are then sent to him for examination as to the question of sinus origin. It is seldom, therefore, that the rhinologist sees a condition which is not of such origin. I shall report 2 cases in a fairly large series which illustrate a number of features that are in dispute.

A youth whom I first saw in 1925, at the age of 16, had had a cold three weeks before. Four days before he consulted me he had blurring of vision in the right eye. An ophthalmologist, the late Dr. Isadore Goldstein, made a diagnosis of right retrobulbar neuritis and referred him to me for examination of the sinuses. Both the clinical and the roentgenographic examination afforded evidence of bilateral ethmoiditis and right sphenoiditis. I treated him conservatively for two weeks with irrigation and other methods. Vision in the eye gradually improved, and at the end of three weeks there was no evidence of disease. Five years later he returned with the history of a cold three and a half weeks before. Vision in the right eye had been blurred for two weeks. I treated him for three weeks, this time with no improvement. Dr. Goldstein insisted that the sinuses should be opened. I did a right ethmosphenoidectomy and observed pus in the sinuses. When the operation was finished, the patient said: "My eye is better," and from then he showed improvement; in two weeks vision was normal. Two months after the operation the patient said that vision in the left eye was becoming blurred. Dr. Goldstein found retrobulbar neuritis in the left eye. I treated the patient for a week, and then opened the sinuses on the left side. The previous experience was repeated; vision cleared up promptly.

It is thirteen years since the original attack. He has had no further evidence of trouble with the eyes, is healthy and has no evidence of multiple sclerosis. I think one must regard the condition in this case as true rhinogenic retrobulbar neuritis that involved both eyes.

About a year ago I had a unique experience. A middle-aged man was referred from the neurologic service of Dr. Strauss for treatment of foci of infection because of pains in the lower part of the back and legs. Neurologic, ophthalmologic and general examinations gave essentially normal results. One of my assistants did a right sphenoethmoidectomy because of bilateral disease of the sinuses. Nothing untoward occurred until he removed the anterior wall of the sphenoid sinus; an unusually large vessel bled profusely, but the bleeding was quickly stopped. A few days later the left side was operated on. The patient likewise had profuse hemorrhage on this side, and this time the surgeon had to pack the sphenoid sinus. The packing was left for two days and removed. On the following day the patient said he had blurring of the left eye. He was examined by Dr. Schlivek, who made a diagnosis of left retrobulbar neuritis. There were a slight amount of ecchymosis of the left upper and lower lids and blood clot and pus in the left sphenoid sinus. The sinus was cleaned, and within two weeks vision returned to normal. In this case there was essentially experimental production of retrobulbar neuritis of nasal sinus origin as the result of packing, possibly associated with hemorrhage and infection, the latter spreading along the lymphatics into the orbital tissues. I do not see how there can be any doubt as to the connection between the nasal sinus and the retrobulbar neuritis in this case. One of the reasons advanced for the lack of correlation between disease of the nasal sinuses and retrobulbar neuritis is that the latter does not occur in children. However, it does occur; there are two reasons for its infrequency in children: First, the sphenoid sinus and the posterior ethmoid cells in children are, as a rule, slightly or partially developed, and, second, the sphenoid and ethmoid sinuses are, unlike those in the adult, comparatively far removed from the optic nerve and its accompanying vessels.

As to treatment: In all cases of optic neuritis operative intervention is not required. If damage to the eye has not lasted long and is not progressive, irrigation of the sphenoid sinus and other conservative measures are often successful in effecting a cure. The ophthalmologist must observe the progress of the con-

dition of the eye frequently and carefully; only when advancement of the neuritis or marked involvement of the optic nerve is present is it necessary to operate. Estimation of the damage to the eye, of the progress of the disease and of the possible effect in the production of optic atrophy is a problem for the ophthalmologist; he must decide when conservative measures are to be discarded for operative procedures. The rhinologist acts only as a technician for the neurologist and the ophthalmologist in the treatment of optic neuritis.

Dr. Eric Miles Atkinson: This is a vexed question—that of how far infection in the sinuses affects the optic nerve. I am heartily in agreement with Dr. Schlivek on the importance of differentiating between optic and retrobulbar neuritis. Dr. Needles mentioned Traquair, of Edinburgh, as expressing the opinion that retrobulbar neuritis of rhinogenic origin is an extremely rare complaint. That is, I think, the accepted opinion in most clinics in England. Many evils have been laid at the door of the sinuses, and at that of the rhinologists incidentally, and I think this is one of them. When I was working at one time in a large clinic in London my colleagues and I investigated this matter. We asked ophthalmologists to send to the nose and throat clinic every patient with retrobulbar or optic neuritis for rhinologic investigation; of more than 200 persons examined we found 3, or at least under half a dozen, in whom there was any evidence of disease of the sinuses. There was at that time a great deal of talk about "cryptic" sinusitis. It was so cryptic that most persons could not find it. Watson Williams used to advocate puncture of the sinuses, culture of the washings, operation and vaccine therapy on what seemed flimsy evidence of infection; he said that he cured optic and retrobulbar neuritis. Retrobulbar neuritis in many instances ends in spontaneous recovery. I believe that rhinogenic retrobulbar neuritis is extremely rare, and rhinogenic optic neuritis is not much more common. Still, if with unilateral optic neuritis there are found definite evidence of pus and roentgenologic signs of sinus disease, I believe the patient should be given the benefit of surgical treatment. Whether he recovers as a result of surgical intervention or in spite of it, I am not prepared to say.

Dr. Irving B. Goldman: The rather characteristic picture that one obtains in cases of sinusitis associated with optic or retrobulbar neuritis is the lack of suppuration. There is not the typical picture of purulent sinusitis, and that makes the diagnosis difficult. As a fact, in the first case of bilateral optic neuritis reported tonight, the right sphenoid sinus was irrigated at first and the return fluid was practically clear; however, when the sphenoid was opened mucocele was observed. The man was seen several months after the operation; vision had returned, and he was able to resume work. In this group of cases it will be noted that most of the patients were operated on in the spring, summer or fall, not at the time when infections are most common. I had the experience recently of operating on a man with macular edema. The roentgenograms of the sinuses showed nothing abnormal, and rhinologic examination revealed little; nevertheless, operation on the sphenoid sinus disclosed a scant amount of thin pus from which a hemolytic streptococcus was cultured. He had return of vision after the operation. When one considers all these cases, one cannot escape the conclusion that if there is no other focus of infection one must investigate the sinuses.

Dr. Israel Strauss: I expected a divergence of opinion when the paper was read. I was fully conscious of the views held by ophthalmologists and rhinologists but not by neurologists, because they have not taken much part in the discussion of this problem. Here is a field in which the three specialties meet. There is a frequent difference of opinion among ophthalmologists as to what constitutes an inflammatory condition of the optic disk as differentiated from changes due to increased pressure of intracranial origin. The problem is not whether it is optic or retrobulbar neuritis. It may be true that in many cases retrobulbar or optic neuritis is cured spontaneously. When the physician finds a situation, however, in which there is impairment of vision, for the cause of which he is looking, and

when on careful examination he finds nothing that he can ascribe to inflammation or disease of the central nervous system, is he therefore to sit back and let events take their course, or should he go further and look for something as a cause: a possible infection outside the central and the peripheral nervous system? In looking for the possible cause he goes, naturally, to the site nearest the optic nerve; he investigates the sinuses. That is what has been done, and the results in some cases have been excellent. Sometimes we were uncertain of the ultimate outcome because we were unable to follow the patients as we should like to have done. If by this method, however, we have preserved the vision of 1 patient only we have done what a physician should.

I shall refer to the case which was described as one of "sphenoiditic hydrocephalus." I am not certain that one should characterize it in that way, although in reviewing the literature I found that internal hydrocephalus has been reported as resulting from infection of the sinuses, in the absence of any other focus. The patient suddenly experienced a symptom complex of meningitis after an operation, cyclopropane being used as the anesthetic. At that time no lumbar puncture was made. When examined several days later, the woman complained of severe headache and radicular pains on the right side of the body, involving the arm and shoulder. Examination revealed signs of multiple neuritis of the extremities and a high degree of choked disk, i. e., real papilledema, or optic neuritis, with blindness. We expressed the belief that it was not an intracranial condition. The process advanced; the papilledema or optic neuritis increased, and hemorrhages appeared. Blindness increased. Finally, when it was learned that she had been treated previously for sinal infection, lumbar puncture was performed. This revealed a pressure of 500 mm. of water and an Ayala index of +6, which was against the probability of an expanding lesion. Dr. Goldman was consulted, and he operated on the sphenoid sinus, finding a suppurative process. At the second lumbar puncture the pressure had fallen to 300 mm. of water, and at the next puncture, to 100 mm. Today the patient's condition is normal.

Another case was even more striking, that of a boy who complained continuously of intense headaches; he could not read. Vision seemed normal. One day he stated that vision was not good, and I noted the beginning of blurring of the disks. Roentgenograms showed slight clouding of the sinuses. Dr. Kramer opened the sphenoid sinus. The front portion was clean; then he discovered a ridge, behind which there was pus; this was removed. The blurring of the disks and headaches disappeared, and the boy is well.

Whether one calls a condition retrobulbar neuritis or optic neuritis, when the patient is in danger of loss of sight (with or without multiple sclerosis) and a focus of infection in the sinuses is found by a reputable rhinologist the sinuses should be treated by the rhinologist in an approved manner, thus giving the patient the benefit of the doubt.

Dr. William Needles: I wish to mention one point. I recognize that it is desirable to differentiate between optic and retrobulbar neuritis, but I wonder if it is always possible. Is it not common for a process to start in the retrobulbar portion of the nerve, spread forward and produce optic neuritis? Conversely, is it not common for a process to start at the papilla as optic neuritis and spread back to produce retrobulbar neuritis? Is it not possible that the presence of optic neuritis masks the presence of retrobulbar neuritis?

Disturbances of Perception and Relation to Disturbances in Posture.

Dr. F. A. Quadfasel (by invitation).

The disturbances of perception considered in this paper form a special group between the agnosias, in the narrow sense of the word (i. e., inability to recognize an object or picture), and disturbances of sensation. The disturbances of percep-

tion consist of: (1) displacement of objects from the vertical or the horizontal position in a regular way; (2) distortion in the shape of geometric figures; (3) change of the spatial threshold for optic and tactile stimuli (the patient is not able to see a line of dots as such or to recognize papers of different roughnesses), and (4) disturbance in the appreciation of brightness.

The disturbances have occurred in association with cerebellar lesions, definite vestibular symptoms and general disorders (arteriosclerosis of the brain, multiple sclerosis and atypical migraine). They have been described by von Weizsäcker, Goldstein, Feuchtwanger and Quadfasel (Hoff, Hans: Die zentrale Abstimmung der Sehsphäre, Berlin, S. Karger, 1930. Kleint, H.: *Ztschr. f. Psychol.* **138**:1, 1936; **140**:109, 1937; **141**:9, 1937; two more parts to be published. Quadfasel, F. A.: *Monatschr. f. Psychiat. u. Neurol.* **96**:326 [Aug.]; **97**:90 [Sept.] 1937). They may be present unilaterally or bilaterally. The patient may, for example, see a chimney leaning to one side. It is usually possible to reproduce these phenomena by asking the patient to place a line, drawn on paper, vertically or horizontally in front of him. A deviation of about 10 degrees is found. (The normal deviation is not over 1 degree.) The displacement may be unidirectional or in opposite directions in the vertical or the horizontal plane. It may be more marked in the vertical. Geometric figures are distorted accordingly. Squares are seen as rhombuses, circles or ellipses.

The disturbances of perception depend on certain conditions: the size of the object, the stability of the figure, the background and the attitude of the patient. These conditions explain why the patient in ordinary life does not see the whole of his external world as slanting or inclined.

Disturbance of posture is always present in patients with these disturbances of perception. The posture of the arms when stretched forward is not maintained for any considerable time. The arm drifts or rises to a new position of balance.

The relation of disturbances of perception to those of posture is described: 1. The disturbance of perception occurs on the side of the drifting arm. 2. Change in the position of the limbs influences the disturbance of perception. Other stimuli affecting the tone of the musculature, such as colors, are mentioned, and their influence is shown.

The occurrence of these symptoms on one side, the selectivity of symptoms and the association with frontal and cerebellar lesions point to the conclusion that definite pathways are concerned. Neither vestibular nor cerebellar lesions need be present.

Conclusions.—1. These phenomena represent a definite type of disturbance of perception, which must be differentiated from agnosias and cerebral metamorphopsias. They do not constitute a disturbance in *Gestalt* formation. The patient distinguishes the "vertical," the "figure" and the "thing."

2. The factor concerned has been called a "tonic component." Its importance in certain perceptions has been shown experimentally, in normal persons and in patients with this disturbance. It represents a component of the "spatial framework." 3. Perception is not an isolated performance of a single sense organ. Optic, tactile, vestibular and tonic components influence what actually appears in one's evironment as one perceives it. They always act as a whole and therefore are interdependent and represent what has been called the wider visual area. 4. The disturbance of the tonic component expresses itself in the disturbances of perception described. The "framework" has become unstable. 5. It is important to stress that these disturbances of perception, like those of the vestibular and cerebellar type, are homolateral, as opposed to those of the type resulting from a lesion in the occipital lobe. This group may therefore be called homolateral metamorphopsias. 6. Some functions of the brain are more closely related to each other than are others, and it is more productive to search for this mutual relationship than to consider the brain as acting as a whole.

DISCUSSION

DR. PAUL SCHILDER: It is not simple to discuss a paper which deals with the basic psychologic and psychopathologic problems of perception. I believe that in the first case of Weizsäcker's (Ueber einiger Täuschungen bei Erkrankung des Vestibulärapparates, *Deutsche Ztschr. f. Nervenh.* **64**:9, 1919; Ueber einer systematische Raumsinnstörung, ibid. **84**:179, 1924) in which the distortion of optic perception was observed the lesion was a cerebellopontile one; there was sufficient evidence to implicate the nucleus of Deiters. I suspect that many instances are based on lesions of the central vestibular apparatus. With Hoff (Hoff, H., and Schilder, Paul: Zur Kenntnis der vestibulärer Erkrankungen, *Deutsche Ztschr. f. Nervenh.* **103**:145, 1928. Schilder, P.: The Vestibular Apparatus in Neurosis and Psychosis, *J. Nerv. & Ment. Dis.* **78**:1 [July] 1933), I have studied a case that belongs in this group. The patient had an outspoken disturbance of this type in one eye and a less definite disturbance in the other. It should be emphasized that the patient also experienced movements in his optic perceptions, especially on the more severely affected side. The patient also had marked deviation in posture; the postural reflexes were abnormal. Autopsy revealed a destructive process in the inner ear and meningeal infiltration which reached the region of the nucleus of Deiters. It is probable that many of these disturbances are due to unilateral lesions, especially in the nucleus of Deiters or the central vestibular apparatus. It is difficult to appreciate in detail the relation between tonus and the visual disturbances in these cases. It is probable that changes in tonus evoke immediate distortion of the visual world. This becomes clearer when one recalls that when the ear of a normal person is irrigated he will experience not only apparent movement but also a change in the position of objects seen in space. Under such conditions, distortion and changes in spatial relations affect not only optic perceptions but optic imagination. There is no question that vestibular tone has an influence on perception. The exact nature of its influence is difficult to define. Vestibular tone is only one of many variants of tonus. I think that many of the phenomena involved here are in close relation to the apparatus for tonus of different levels. I mentioned the tonus which occurs on stimulation of the vestibular apparatus, with its specific influence on perception. There is, furthermore, the state of tone noted in connection with cerebellar lesions, which changes perception too, and there are all the variations of tonus which accompany the postural and righting reflexes. Specific postural apparatuses have specific influences on optic perception and optic imagination. The postural apparatus has its highest station in the parietal and optic lobes. Associated with lesions of these parts of the brain one finds changes in tone and disturbance in optic perception. I think one can adopt a unified concept concerning the relation of motility and tone, especially in relation to optic perception. Every step and every level of this apparatus have a specific influence on perception. This has, of course, a far reaching bearing on the whole problem of visual perception. Such phenomena are present not only in the optic but also in the tactile sphere, as Bromberg and I have shown.

In conclusion: One should not consider experiences of this type as extraordinary. For many years I have experimented with visual imagination. In visual imagination distortion similar to the observations of Dr. Quadfasel can be found, especially if one tries to retain the optic images for a long time. Many changes take place, and they increase and diminish according to the general status of motility and tone. The interesting observations by Dr. Quadfasel show particularly the connection between the perception and apparatus for tonus. However, phasic motility also has an important bearing on perception. This is a new field, in which interesting work may be expected. These phenomena are of importance, since they point to changes in the vestibular apparatus or in the apparatus which serves tone.

DR. I. S. WECHSLER: It seems to me that Dr. Quadfasel has complicated a problem which needs simplification. Dr. Schilder alluded to postural reflexes, and I should add the righting reflexes, but I should place them at a much higher level.

I think one is dealing here with the highest type of reflexes described by Magnus and de Kleyn, namely, the optic righting reflexes. It is known that tonus and posture are maintained by the righting reflexes, and there is reason to believe that these reflexes play a role in the conditions described by Dr. Quadfasel. In the case of the tonic neck reflexes, the posture and tonus of the limbs vary with the position of the head. Whether the ipsilateral or the contralateral limbs become hypertonic and extended depends on whether the head is rotated or bent to the side. If one rotates the head, the extension and rigidity are on the side toward which the chin points, and the flexion is contralateral. The reverse happens in bending the head to the side. Magnus has shown this in experiments on animals. The recent work by Fulton and Bieber has shown the influence on posture and tonus of direct injury to bilateral premotor areas.

I doubt whether orientation, such as Dr. Quadfasel has in mind, can be relegated to such low levels. Not that the cerebellum and the vestibular apparatus have no influence on tonus or posture; I do not think, however, that spatial orientation can be attributed to them. There are definite clinical and pathologic observations on patients who have received injuries to the cerebral cortex near the supramarginal gyrus, in the region between the parietal and the occipital lobe, who showed spatial disorientation. Many years ago, Gordon Holmes described cases in soldiers with bilateral injuries of the brain, in the areas mentioned, who lost spatial orientation. Some time ago I cited before this society the case of a cabinet maker who, after a blow on the head, lost the ability to measure depth and length, whereas before the blow he could tell accurately the thickness of board, within ⅛ inch (0.32 cm.). After the injury he lost completely the ability to measure distance and could not tell the difference between a board 1 inch (2.54 cm.) and a board 3 inches (7.62 cm.) in thickness.

It is also known that in cases of intoxication, in which the influence is on the cortex, orientation in time and space is disturbed. Hashish poisoning is the best example of such disorientation. It was clear that the postures demonstrated by Dr. Quadfasel varied with the position of the head and with closing the eyes. Disregarding the influence of the ocular muscles, one may conclude that the postures which he discussed and the illustrations which he showed may be correlated in large measure with the optic righting reflexes.

Dr. Walter Boernstein: Dr. Quadfasel has shown that in certain patients with disturbances of tone the perception of straight lines is influenced by the state of tonus present in the head, trunk and extremities. Dr. Schilder, stressing this fact, asserts that the connection between body tone and ocular perception is provided by the vestibular apparatus.

At the Physiologic Institute at Frankfort on the Main, Germany, I proved experimentally that muscles and retinal cones are not "connected" by any third, intercalated system but that the retinal cones are part of the tone apparatus itself, reacting to the same stimuli in the same way as the muscles.

Previously, I had shown that every stimulus of bright light increases body tonus. I expected that such stimuli, acting on the skin, would also cause contraction of the cones—perceived as light. I kept healthy subjects in a dark room for forty-five minutes and then exposed their backs to ultraviolet rays (the eyes, of course, were kept in complete darkness during the whole experiment). In each case the persons saw bright light about fifteen seconds after irradiation of the skin was begun. This and other experiments prove that, in respect to tone, the cones of the retina are functionally identical with the muscles of the body.

Dr. Moses Keschner: I wish to know whether the patient with deviation of the right upper extremity had any objective evidences of disturbance of the sense of position of the fingers and hand in that limb.

Dr. F. A Quadfasel: No.

Dr. Donald Gregg: I have been observing a patient with a condition diagnosed as multiple sclerosis who has what may be called kinesthetic amnesia. The patient

shows marked inability to remember slight motions with which she should be familiar. No matter how many times she turns on the radio, she cannot remember how to manipulate the dial—whether to the right or to the left—to get the station she wishes. She cannot remember whether the faucet in the bathroom turns to the right or to the left and which way to turn the key in the door. There is almost complete amnesia to the small motions which most persons learn after a while.

As memory plays a part in agnosia, I wish to ask Dr. Quadfasel whether there is any evidence of amnesia as regards motion in his case and whether he has tested his patient's ability to recognize the perpendicular with eyes closed.

DR. F. A. QUADFASEL: I agree with Dr. Schilder that this syndrome is not rare. Unfortunately, it has been described in detail in few cases. Von Weizsäcker described it in three papers. His first patient had a vestibular lesion; he concluded, therefore, that this was responsible for the symptoms. In his last paper, in 1931, however, he had given up this point of view and spoke of a metaorganic realm of function, assuming a change in frequency of impulses on one side of the body. He did not see the relationship between perception and tone, although such disturbances were present in his cases. He did not regard these symptoms as a localized disturbance, but concluded that they were due to a disturbance in function of an entire half of the brain.

These disturbances can be found in cases of frontal, cerebellar and vestibular disease, but such lesions need not be present; moreover, disturbance of a tonic component is related to such deviations in normal persons and in patients with disturbances in perception.

In answer to the remark that these disturbances are of the highest level, I wish to point out that it is not yet known why one can judge vertical and horizontal lines so much better than lines at any other angle—facts which were investigated in this country by Jastrow (*Am. J. Psychol.* **5**:214, 1892). In later years Hofmann and Froboese (*Ztschr. f. Biol.* **80**:91, 1924) performed careful experiments on the possible causes. They excluded the sensation of the position of the head and body, the perception on vertical meridians of the retina and the motility of the eyes and came to the conclusion that ability to judge a vertical line depends on ability to judge the direction of gravity through sensations coming from the head. Hofmann concluded that sensations arise from the organ of balance. Gelb explained the disturbances by changes of tone on one side of the body. Our cases support his point of view.

Wilder, who described such disturbances of perception, came to the conclusion that monocular deviations from the vertical occur in cases of peripheral lesions, and only "sometimes perhaps" in those of cerebral lesions. I wish to stress the necessity of differentiation of central metamorphopsias of the type resulting from lesions of the occipital lobe and these homolateral metamorphopsias.

I cannot say anything here about the question of "amnesia of movement." I think that is a different problem from the one considered here.

Book Reviews

Report of the Assistance of Indigent Patients Suffering with Epilepsy. The Minnie Frances Kleman Memorial Fund. Northwestern University Medical School, the Department of Nervous and Mental Diseases, Chicago. Not for sale. Cloth. Pp. 567, with illustrations. Ann Arbor, Mich.: Edwards Brothers, Inc., 1936.

This book is a private report from the Northwestern University Medical School to the officers of a foundation which gave grants for the "assistance of indigent patients suffering with epilepsy." The work includes a collection of interesting studies, many of which have appeared or will appear in the current literature on neurology and psychiatry. The purpose of the report renders wise the inclusion of a brief historical outline of facts about epilepsy, especially the use of the word idiopathic, and a discussion of the problems of etiology and therapy.

The detailed work of the medical school concerned the study of 96 patients. Brief abstracts of the case histories are presented. Clinical and laboratory studies were made of the urine, blood and spinal fluid and of the effects of anoxia and hyperventilation. Sugar, water and other forms of metabolism were investigated. Gonadotropic substances were isolated. The data were analyzed in relation to sex, age, the duration and nature of attacks, auras, heredity and other factors. Abnormal roentgenographic and ventriculographic findings are reproduced; these refer largely to intracranial calcifications and enlarged ventricles. Therapeutic agents, including ketosis, snake venom, drugs, water restriction and surgical intervention, were investigated. Psychometric studies on the patients add an interesting chapter. Literature dealing with physiochemistry is reviewed, and the need for more extensive investigation is emphasized.

The book makes no claim to major discovery. The material is presented as evidence of a systematic and well planned study of a complex problem and should be adequate to convince the trustees of the fund that the grant has been made wisely.